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THE NATURE OF SPONTANEOUS AURICULAR FIBRILLATION IN MAN

WITH COMMENTS ON THE ACTION OF ANTIARRHYTHMIC DRUGS

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Although auricular fibrillation is one of the commonest and most serious disorders of the human heartbeat, its mechanism in man has not yet been demonstrated. Direct observation of the arrhythmias has heretofore been confined largely to that done on experimental animals. Flutter and fibrillation were produced in dogs by a variety of methods, including electrical, chemical, and mechanical stimulation.[1] Some of these methods showed disorders that appeared to involve a circus movement[2]; on the other hand, some instances of flutter and fibrillation were found to result from a rapidly discharging ectopic focus.[3] Thus the mechanism of arrhythmias observed in laboratory animals may vary with the method of production. Because of this limitation of the experimental approach, the only reliable means for determining the nature of clinical auricular fibrillation is to observe the disorder as it actually occurs in human hearts. Evidence obtained directly from the fibrillating auricles of patients constitutes the subject of this report. Experimental data from laboratory animals are cited only insofar as they elucidate certain observations in man.

DIRECT OBSERVATIONS ON SPONTANEOUS AURICULAR FIBRILLATION IN MAN

Recent advances in cardiac surgery have made feasible for the first time a direct approach to the question: What is the nature of spontaneous auricular fibrillation in man? During the past several years, many patients with previously intractable valvular disease and auricular fibrillation have benefited from mitral commissurotomy. The surgical procedure necessitates exposure of the auricles, thereby providing an excellent opportunity for direct observation. On 15 occasions, specially designed electrocardiographic or motion picture equipment was introduced into the operating room and prepared for immediate use. The surgeon then opened the patient's chest, resected the ribs, and opened the pericardium. After the fibrillating auricles had thus been exposed, about 15 minutes was devoted to making direct auricular leads or slow motion pictures in color before the commissurotomy was performed. These records constitute the most direct evidence of the nature of auricular fibrillation in man that has yet been obtained.

Auricular Leads.—In each of nine patients, direct auricular leads were recorded from cotton-tipped electrodes tied to the fingers of the operator. Rubber gloves insulated the operator's hands from the electrodes. Tracings from the left and right auricles were recorded simultaneously in four instances. Simultaneous leads from two sites on one auricle or from the auricle and the left ventricle were made in the remaining cases. All leads were registered on a Sanborn Twin-Beam Cardiograph at a paper speed of 25 or 75 mm. per second. Two general types of waves appeared in the direct leads, large and small (fig. 1). The large waves occurred at rates of 250 to 400 per minute. They usually showed intrinsic-like downstrokes. In seven cases, the rate of occurrence of the large waves was irregular and each wave differed from the others in size and shape. Large waves of relatively constant size and shape occurred at a regular rate in the remaining case. Throughout all the tracings, highly irregular, small waves appeared as peaks or undulations along the baseline and on the upstrokes and downstrokes of the large waves (fig. 2). These small waves were never recorded in control tracings or in ventricular leads. Esophageal lead oscillograms from 24 patients with spontaneous auricular fibrillation showed large and small waves comparable to those in the direct leads.[4] The large waves in direct and esophageal leads during fibrillation are responsible for the irregular F waves in limb lead tracings. The small waves cause the grass-like appearance of the baseline in the limb leads.

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A noteworthy feature of the direct leads concerns the auricular rate. Since tracings from the left and right auricles were recorded simultaneously in four patients, the left and right auricular rates could be compared. In three of these patients, the large waves occurred at more rapid rates in leads from one auricle than in leads from the other auricle (fig. 3 and table). This indicates that one auricle beats faster than the other. If a single circus movement involved both auricles, they would have to beat at the same rate. It is unlikely that separate circus movements could occur in the left and right auricles, since the bodies of these chambers are connected by continuous muscle fibers throughout most of their course.[1r] Even if separate circus movements were present in each auricle, the rate would have to be the same. Otherwise, daughter waves arising from the more rapidly beating auricle would invade the opposite auricle, where they would interrupt the circus movement. Thus the difference between left and right auricular rates appears incompatible with circus movements of any size. The configuration of the large waves also conflicts with the circus movement theory. If a circus movement were present, the impulse would return toward the electrode after passing it, and the returning wave would be recorded in at least some of the tracings, even if the circus pathway were highly irregular. Actually, no such returning impulse was ever registered The large waves were purely negative, purely positive, or positive-negative. This indicates that the impulse traveled away from the electrode during some beats, it traveled toward the electrode during other beats, and it sometimes traveled toward the electrode, passed, and then traveled away. On no occasion was the impulse found to pass the electrode and return during the same beat, as it should if a circus movement occurred (fig. 4).

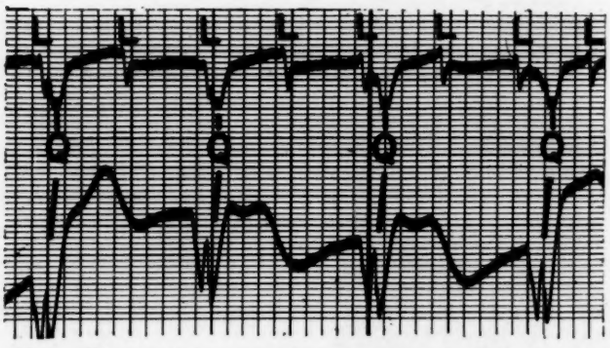

Fig. 1.—Direct leads from exposed right auricle (upper tracing) and left ventricle (lower tracing) of patient with spontaneous auricular fibrillation. Right auricular lead shows large waves (L) occurring at irregular rate of 300 per minute. Q waves following alternate L waves represent effect of ventricular. deplorization on auricular lead. Note that each auricular L wave presents intrinsic-like downstroke.

Auricular Waves Discharged per Minute

Left	Right
298	318
282	318
282	309
300	312
291	309
297	319
Average 292 (SD ± 7.37)	Average 314 (SD ± 4.30)
Range 282 — 300	Range 309 — 319

High-speed color motion pictures made of two patients with auricular fibrillation before removal of the auricular appendix were described in 1951.[1t] Since that time, a similar technique has been used to photograph the fibrillating auricles of six patients before mitral commissurotomy. The motion of the left auricular appendix in these instances was limited because of congestion due to mitral stenosis. By pushing down the pulmonary artery, the right auricle could be clearly visualized. In the right auricular appendix, more or less organized contraction waves were observed. The contraction waves correspond to the large F waves in the fibrillation electrocardiogram. They occurred at irregular rates of 250 to 400 per minute. Each large wave differed from the preceding wave in course, in vigor, and in speed. When the motion pictures were carefully examined, a second type of mechanical activity could be seen. This consisted of rapid, heterorhythmic, weak contractions and dilatations of minute muscle segments occurring constantly throughout the appendix simultaneously with the larger waves. The weak contractions appear to be counterparts of the small waves in the electrocardiograms. They were most clearly demonstrated

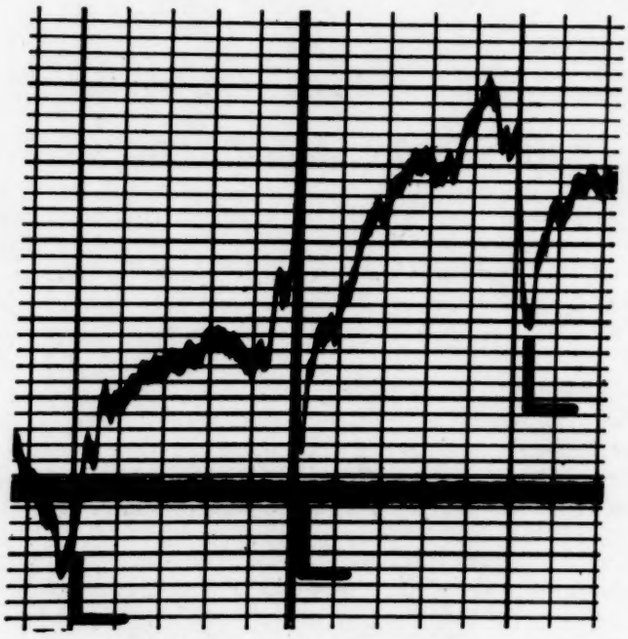

Fig. 2.—Direct lead from right auricle of patient with spontaneous auricular fibrillation, magnified 2.5 times. Small waves of variable configuration occur at extremely rapid rates along baseline as well as on upstrokes and downstrokes of large waves. These small waves correspond to irregularities of baseline seen in figure 1 and in limb leads during fibrillation.

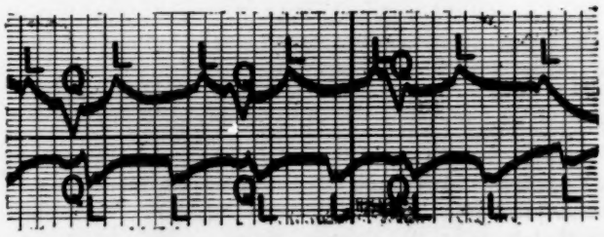

Fig. 3.—Simultaneously recorded direct leads from left (upper tracing) and right auricles (lower tracing) of patient with spontaneous auricular fibrillation. Large waves (L) in left auricular lead occur at slower rates than those in right auricular lead. If circus movement were present, left and right auricular rates should be equal (see table).

at the tip of the appendix, where the fimbria twisted and turned in an entirely uncoordinated manner. For purposes of description, the appearance of the fibrillating auricles may be likened to a storm at sea. Nothing is visible that resembles a circus movement, an isoelectric gap, or daughter waves.

MECHANISM OF AURICULAR FIBRILLATION

The widespread belief that spontaneous auricular fibrillation in man shows a circus movement was derived largely by analogy with experimental flutter, not by direct observation. This belief has prevailed since Lewis' classic study of auricular flutter in dogs gave evidence of a self-perpetuating circus movement.[1a] Although Lewis also studied fibrillation, he found it impossible to analyze the path of the fibrillary wave because of marked variations in the auricular complexes. Nevertheless, the close relationship between flutter and fibrillation suggested that fibrillation also results from a circus movement. From recent evidence, two limitations of this assumption have become apparent: (1) that experimentally produced arrhythmias may differ in mechanism from one another and from spontaneous arrhythmias[5]; and (2) that, in patients with auricular flutter, arrhythmias resulted from a rapidly discharging ectopic focus rather than from a circus movement.[9] Esophageal leads from multiple auricular levels were recorded from many patients with spontaneous auricular flutter. The configuration of the complexes indicates that each flutter wave arose from an ectopic focus at one end of the auricles, traveled through both auricles simultaneously to the opposite extremity, and then terminated. None of the tracings showed evidence of the returning impulse that is essential to circus movements. In limb leads, the undulatory pattern of clinical flutter is often attributed to a continuous circus movement. An analysis of over 100 such tracings, however, showed that the flutter complex did not represent a circular pathway. Instead, each complex was found to consist of two well-known electrocardiographic waves; a wave of depolarization followed by an oppositely directed wave of repolarization. Since these two waves occur alternately, they give the electrocardiogram its undulatory appearance. Another characteristic of clinical flutter is the frequent presence of isoelectric intervals after the auricular complexes in limb leads. According to electrocardiographic theory, such isoelectric intervals indicate that no electrical activity is present; that is, they apparently represent auricular diastole. Diastolic periods would not be expected to follow each auricular beat if the flutter wave pursued a continuous, homogeneous circus pathway. The sequence of electrical events in the fluttering auricles of man thus does not necessarily suggest a self-perpetuating circus movement. Instead, it may simply consist of depolarization proceeding from an ectopic focus to the extremities of both auricles, then repolarization along the same course, usually followed by an isoelectric period or diastole.

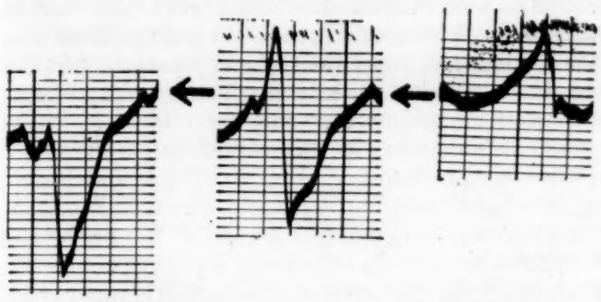

Fig. 4.—Typical large waves recorded in direct auricular leads from patients with auricular fibrillation. Complex at left is negative, indicating that impulse initiated at and traveled away from electrode. Center complex is positive-negative, indicating that impulse traveled toward, passed, and then traveled away from electrode. Complex at right is positive, indicating that impulse traveled toward and stopped at electrode. Each fibrillary wave thus traveled away from its site of origin until it terminated. No returning wave was found.

The mechanical activity of the fluttering auricles in man likewise appears to conflict with the circus movement theory. The motion of the patient's auricles was similar to that of dog auricles during bouts of flutter arising from a rapidly discharging ectopic focus. Both auricular appendixes were clearly visible in the films of spontaneous flutter. They contracted simultaneously and then relaxed simultaneously. If a circus movement proceeded around the venae cavae, one appendix would contract and relax before the other. Simultaneous motion of both appendixes is incompatible with the classic circus movement described by Lewis, but it is exactly what would occur if the flutter wave traveled away from an ectopic focus through both auricles simultaneously. These data, together with the foregoing direct observations on the fibrillating auricles of patients, clearly necessitate a reexamination of the mechanism of spontaneous auricular fibrillation and its relation to other arrhythmias in man.

There is much in common between the electrical and the mechanical activity of normal sinus rhythm and that of auricular extrasystoles, tachycardia, and flutter in man.[1r] The normal beat originates at the sinoauricular node. The extrasystole, tachycardia, and flutter beats originate at an ectopic focus. In all four rhythms, leads from the site of origin of the beat show purely negative deflections; leads from between the site of the origin and the auricular extremities show positive-negative deflections; and leads distal to the site of origin show purely positive deflections. Thus the depolarization waves of normal rhythm and those of the three arrhythmias travel in an orderly manner from the focus to the extremities of both auricles. The contraction waves of all four rhythms pursue the same course as do the depolarization waves. This orderly progression of electrical and mechanical waves has been observed during normal sinus rhythm and during auricular extrasystoles, tachycardia, and flutter, both in dogs and in man. It appears to be a fundamental law governing the auricular muscle that applies not only to normal sinus rhythm but to all auricular arrhythmias except fibrillation. Diagrams of the auricle showing

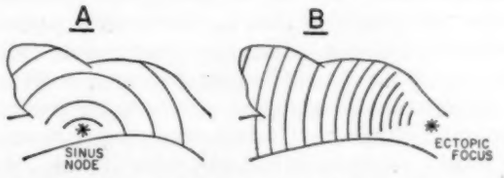

Fig. 5.—*A*, auricle during normal sinus rhythm. Impulse initiates at sinus node and spreads outward in all available directions until it reaches the extremities of the auricles. *B*, auricle during extrasystole, tachycardia, or flutter. Impulse initiates at ectopic focus and spreads outward in all available directions. Note similarity between orderly activation of auricles during these arrhythmias and during normal sinus rhythm.

the orderly course of depolarization and contraction during normal sinus rhythm, extrasystoles, tachycardia, and flutter are shown in figure 5.

The relationship between fibrillation and the slower arrhythmias can be clearly demonstrated in experimental animals. Auricular fibrillation occurs when the rate of discharge from an ectopic focus reaches a certain critical level called the fibrillation threshold. The fibrillation threshold varies in different animals. It is influenced by a number of factors, including the condition of the myocardium, vagal tone, and drugs. But whether the fibrillation threshold is high or low, it is always associated with a complete breakdown of orderly electrical and mechanical activity. Some of the large waves in the fibrillating auricle travel toward the ectopic focus; others travel away from the focus. In contrast, the waves of all other auricular arrhythmias never travel toward the focus. The rate of occurrence of the large waves in the fibrillating auricle usually is more irregular and slower than the rate of stimulation at the focus. In all other arrhythmias, the rate of occurrence of the waves corresponds to the rate of stimulation. Throughout the fibrillating auricle, there occur heterorhythmic, small waves unlike anything seen in other rhythms. The nature of auricular depolarization and contraction during fibrillation appears to be entirely different from that during normal sinus rhythm, extrasystoles, tachycardia, or flutter.

The transition from orderly waves to the chaotic activity of fibrillation occurs gradually as the rate of discharge from the ectopic focus approaches the fibrillation threshold. Diastole grows shorter as the rate increases, allowing the auricle less time to recover between successive beats. Conduction proceeds more slowly and in a less orderly manner. Some waves die out before reaching the extremities of the auricle. When the fibrillation threshold is reached, conduction becomes completely disorganized. Changes in auricular excitability as well as other functional changes probably are associated with the conduction failure. Experimental auricular fibrillation thus represents a breakdown of organized activity occurring when an ectopic focus discharges impulses so rapidly that the auricle cannot respond in an orderly manner.

Several reasons exist for suspecting that spontaneous auricular fibrillation in man is similar to experimental auricular fibrillation produced by electrical or chemical stimulation. Both clinical and experimental arrhythmias show large waves occurring at rates over 250 per minute and heterorhythmic small waves occurring at more rapid and irregular rates simultaneously with the large waves. Both are characterized by a complete breakdown of the orderly activity that prevails during all other rhythms. In fact, direct leads and slow motion pictures of experimental arrhythmia [1f] are essentially identical with those of spontaneous auricular fibrillation in the 15 patients observed during cardiac surgery. Another important similarity between clinical and experimental auricular fibrillation concerns the mode of origin. There appears to be a fibrillation threshold in man as well as in animals. This was observed in five patients whose electrocardiograms showed transitions from flutter to fibrillation.[1f] The fibrillation threshold, the rate at which flutter complexes give way to irregular F waves, ranged from 360 to 432 beats per minute. Such rapid rates presumably do not allow the auricle sufficient time to recover between beats. Conduction failure and associated changes would therefore occur, causing a complete breakdown of orderly activity. This seems to be a reasonable explanation of the origin of auricular fibrillation in those instances that are preceded by episodes of flutter.

Auricular fibrillation often begins in patients after a single extrasystole. The mode of origin of the fibrillation in these instances remains a subject of speculation. If the auricle is already disturbed and irritable, as in elderly persons or in patients with hyperthyroidism, heart failure, or abnormal neurogenic tone, an extrasystole falling within the vulnerable period of the cardiac cycle [7] might precipitate a breakdown of orderly activity. The focus of the extrasystole or another previously inactive focus may then discharge at rapid rates, thereby perpetuating the disturbance. Clinical auricular fibrillation thus may begin under two circumstances: when the rate of discharge from an ectopic focus reaches the fibrillation threshold, or when an extrasystole occurs in an irritable auricle during the vulnerable period. Age appears to be an important factor in determining whether fibrillation will begin. The arrhythmia is relatively uncommon in young persons and is rare in infants, even in those with extremely rapid auricular rates or with hyperthyroidism or heart disease. On the other hand, fibrillation often develops in elderly patients, although no specific causative condition can be identified. This suggests that the normal tendency to orderly auricular function may weaken with age, thereby decreasing the resistance to fibrillation. Auricular activity in old persons may become completely disorganized either spontaneously or as a result of minor disturbances, while it remains orderly in young persons despite the presence of profibrillary conditions.

Auricular fibrillation is most frequently associated with mitral stenosis in young patients and with arteriosclerotic or hypertensive heart disease in older patients. Nevertheless, a variety of other profibrillary conditions may be mentioned, including auricular infarction, metastases to the auricles in patients with lung cancer, thyrotoxicosis, surgical procedures, and abnormal neurogenic tone. The fact that such diverse conditions often precipitate auricular fibrillation suggests that the nature of the ectopic focus differs in different patients; for example, "neurogenic" fibrillation may result from a different type of ectopic focus than does fibrillation associated with mitral stenosis, auricular infarction, or metastic cancer of the auricle. The focus in familial cases of fibrillation may differ from that in postoperative fibrillation. These probable variations in the nature of the ectopic focus would explain why auricular fibrillation occurs clinically with a wide variety of structural and functional disorders. It appears less reasonable that such dissimilar conditions could all give rise to the specific combination of circumstances prerequisite to circus movements. A circus movement can occur only if the circus pathway is long enough, the conduction velocity slow enough, and the refractory period long enough to maintain an excitable gap. The muscle enclosed by the circus pathway must be refactory or incapable of conduction owing to structural defects in order to prevent short circuits. Daughter waves must arise from the main pathway to activate the remainder of the auricles. All these circumstances may exist coinci-

dentally in some patients. That they would exist in a large proportion of the many patients with auricular fibrillation arising from diverse structural and functional disorders seems quite unlikely.

A quinidine-induced change from fibrillation to flutter can be observed in most patients if electrocardiograms are made at frequent intervals between the institution of therapy and the restoration of normal sinus rhythm. This further suggests that clinical fibrillation, like flutter, may result from a single, rapidly discharging ectopic focus. The transition from fibrillation to flutter is attributed to a gradual slowing of the rate of discharge from the focus. As the rate drops below the fibrillation threshold, the process of breakdown that marks the onset of fibrillation presumably occurs in reverse. The auricle again has sufficient time to recover between beats, activity becomes more organized, and the irregular fibrillary waves are replaced by regular flutter complexes. Normal rhythm recurs when the ectopic focus finally becomes inactive.

ACTION OF ANTIARRHYTHMIC DRUGS

Whether an arrhythmia results from an ectopic focus or from a circus movement may seem at first glance to have little practical importance. This view neglects the fact that treatment cannot be rational unless the mechanism of the disorder is understood. In order to use antiarrhythmic drugs with maximum effectiveness, the physician must not only be familiar with didactic rules that concern indications, contraindications, dosage, and methods of administration but should also know how each drug affects the myocardium and how its action brings about clinical changes. Although definite answers to these questions must await further pharmacological study, certain tentative conclusions may be drawn from the available data. The following discussion of drug action should therefore be of interest to readers concerned with practical as well as with theoretical aspects of arrhythmic therapy.

Quinidine and procaine amide (Pronestyl) are the most effective antiarrhythmic agents now in general use. Extensive clinical experience with quinidine has shown that the outcome of therapy depends on proper dosage. Large doses often terminate arrhythmias after smaller doses have failed. Similarly, recurrence of the arrhythmia usually can be prevented with adequate maintenance doses. These well-known clinical features of quinidine therapy have been related to a "blood threshold level."[8] Arrhythmias terminate when the blood concentration of quinidine reaches a certain critical level or threshold that varies in different patients but is relatively constant in the same patient; for example, conversion to normal rhythm may be achieved in one patient when the quinidine blood level reaches 1 mg. per liter. In another case, the arrhythmia may persist until the blood level is as high as 10 mg. per liter. Patients likewise differ markedly with respect to the blood concentration of quinidine required to prevent recurrence. Normal sinus rhythm usually can be maintained by keeping the blood level around 3 to 5 mg. per liter with doses of 0.2 to 0.4 gm. three or four times per day.

Although procaine has long been known to possess antiarrhythmic properties, its toxic effects precluded widespread use until procaine amide was introduced by Mark and associates in 1950.[9] Procaine amide sometimes stops arrhythmias that fail to respond to quinidine. Conversely, quinidine sometimes succeeds after procaine has failed. In general, however, the two drugs are comparable in clinical effect. Successful treatment with procaine amide, as with quinidine, depends on proper dosage. Some patients respond to minimal doses of 250 mg. three times daily while others require several times this amount.

An ingenious explanation of antiarrhythmic drug action was presented by Lewis more than 30 years ago.[10] Drugs were supposed to stop arrhythmias by closing the excitable gap on a circus pathway; thus a drug that increases the refractory period or decreases the conduction time would be antiarrhythmic because it would shorten the gap. Conversely, a drug that decreases the refractory period or increases the conduction time would be proarrhythmic because it would lengthen the gap. If a drug increased both the refractory period and the conduction time, or if it decreased both these factors, its effect on arrhythmias would depend on whether changes in the refractory period or in the conduction time predominated. Lewis' explanation of antiarrhythmic drug action has been widely accepted and used for teaching purposes. In fact, it constitutes one of the most popular arguments in favor of the circus movement theory. This may be attributed to the extraordinary flexibility of the explanation that enables it to reconcile a wide variety of clinical and pharmacological observations; for example, Lewis originally stated that quinidine stops arrhythmias by lengthening the absolute refractory period, thus closing the excitable gap on a circus pathway.[1c] Later pharmacological studies by Love [11] and Lewis,[1h] however, showed that quinidine does not alter the absolute refractory period in either auricles or ventricles. The antiarrhythmic property of quinidine was thereupon attributed to a lengthening of the effective refractory period that was also supposed to close the excitable gap on a circus pathway.[1h] This explanation is often extended to include a lengthening of the relative refractory period. Even if a drug fails to prolong the absolute refractory period, the effective refractory period, or the relative refractory period, it may nevertheless eliminate the excitable gap by increasing the conduction velocity.[1f] On the other hand, as noted by Lewis with respect to quinidine, a drug that decreases the conduction velocity may eliminate the gap, provided it lengthens the refractory period to a greater extent than it prolongs the conduction time. Conversely, a drug may lengthen the excitable gap and thus perpetuate arrhythmias if it decreases the absolute refractory period, the effective refractory period, the relative refractory period, and/or the conduction velocity or if it increases the conduction velocity to a lesser extent than it decreases the refractory period. It follows that a drug would have no effect on the excitable gap if it altered neither the refractory period nor the conduction velocity or if it altered these factors proportionately.

Similar complexities are encountered in applying Lewis' explanation to changes in rate of an arrhythmia. According to the circus movement theory, such changes may result either from changes in conduction velocity or from changes in length of the circus pathway.[1g] A drug

may slow the rate of an arrhythmia by decreasing the conduction velocity, thereby increasing the time required for the impulse to complete each circuit. The same drug may increase the rate of the arrhythmia by shortening the refractory period, thus making a shorter pathway accessible to the impulse. Conversely, a drug that increases the conduction velocity may increase the rate of the arrhythmia if the impulse continues along its original pathway, while it may decrease the rate if the refractory period lengthens so that the impulse is forced to pursue a longer pathway. Changes in rate like changes in rhythm thus would depend on the relative magnitude of change in the refractory period and in the conduction velocity.

Two conclusions may be drawn from the foregoing discussion. First, by assuming a differential effect on the refractory period and the conduction velocity, virtually any outcome of arrhythmic therapy can be reconciled with the circus movement theory. A drug such as quinidine may be proarrhythmic, antiarrhythmic, or clinically ineffective, depending on the relative extent to which it alters the refractory period and the conduction velocity. Second, the circus movement theory cannot be used to predict the outcome of arrhythmic therapy unless drug-induced changes in the refractory period and the conduction velocity are estimated prior to administration. Such quantitative estimates are impossible because a drug may have different effects on different parts, in different doses, and at different auricular rates.[12] Moreover, measurements of refractory period and conduction velocity have been made mainly in dog hearts, which may respond to drugs differently than do human hearts. In view of these and other variables, it is extremely difficult to evaluate the circus movement theory by referring it to factual data concerning antiarrhythmic drug action. Nevertheless, certain respects in which Lewis' explanation appears to conflict with recent clinical and pharmacological observations may be noted. According to the circus movement theory, quinidine exerts both an antiarrhythmic and a proarrhythmic effect. The antiarrhythmic effect is thought to be a lengthening of the refractory period that tends to close the excitable gap on the circus pathway. The proarrhythmic effect presumably is a decrease in conduction velocity that tends to lengthen the excitable gap. Recent studies of the fluttering auricles in dogs[1p] have shown that large doses of quinidine do not lengthen the refractory period any more than do small doses. On the other hand, large doses decrease conduction velocity much more than do small doses. Large doses of quinidine thus could not close the excitable gap on a circus pathway after small doses had failed. Clinically, however, arrhythmias that do not respond to small doses of quinidine usually revert to normal sinus rhythm when the blood level of quinidine is adequately increased.[8c] This is the opposite of what one would expect if quinidine acted in accordance with the circus movement theory.

ECTOPIC FOCUS THEORY IN RELATION TO DRUG ACTION

Several other recent observations indicate that antiarrhythmic drugs do not act on the excitable gap of a circus pathway as is suggested by Lewis. Both quinidine and procaine amide significantly slow conduction velocity in the auricles and ventricles of dogs.[13] Hence these drugs must significantly lengthen the refractory period in order to close the excitable gap or even to prevent its extension. Actually, quinidine appears to have no effect on the absolute refractory period in either auricles or ventricles.[14] Moreover, although quinidine generally lengthens the relative and the effective refractory periods, this change is not always correlated with the outcome of antiarrhythmic therapy. Gilbert and his co-workers [12c] observed that quinidine stopped auricular fibrillation in some animals, without greatly lengthening the relative refractory period, while it failed to terminate the arrhythmia in other animals despite a marked increase in the relative refractory period. Brown [1p] reported that auricular flutter in dogs persisted until the total dose of quinidine reached at least 4 mg. per kilogram of body weight. The effective refractory period, however, ceased to lengthen after the total dose reached 2 mg. per kilogram. Woske and associates [12b] found procaine amide highly effective in terminating and preventing ventricular fibrillation although it altered neither the absolute nor the relative refractory period in ventricular muscle. Since the mechanisms of auricular and ventricular arrhythmias appear comparable,[1v] this observation suggests that the effect of procaine amide on auricular arrhythmias also is not correlated with changes in the refractory period.

In view of the foregoing considerations, several workers have concluded that the circus movement theory of antiarrhythmic drug action may not be generally applicable.[15] The ectopic focus theory provides an alternative explanation that appears somewhat simpler and more consistent with available pharmacological evidence. According to this theory, all clinical arrhythmias are perpetuated by a repetitively discharging ectopic focus.[1r] In all the auricular arrhythmias except fibrillation, each impulse discharged by the focus elicits a single organized beat that spreads outward to encompass the entire auricle (fig. 5*B*). Therefore, these arrhythmias terminate if the focus is inactivated, while they continue at a slower auricular rate if the rate of discharge from the focus decreases. In fibrillation, the ectopic focus discharges impulses so rapidly that the auricle cannot respond in an orderly manner. Fibrillation also reverts to normal rhythm if the focus is inactivated, while it slows or converts to flutter if the rate of discharge from the focus decreases. Drugs thus may stop any auricular arrhythmia by inactivating the ectopic focus, or they may slow the auricular rate by decreasing the rate of discharge from the ectopic focus.

The manner in which antiarrhythmic drugs inactivate an ectopic focus or slow the rate of discharge from it probably involves a depression of its excitability.[1r] Normal rhythm recurs if excitability is depressed enough to inactivate the focus. The arrhythmia continues at a slower rate if excitability is depressed enough to slow the rate of discharge from the focus but not enough to inactivate it. No change in rate or in rhythm occurs if the focus is not depressed. Thus the ectopic focus theory, offers an explanation of antiarrhythmic drug action without assuming a complicated differential effect on refractory periods and conduction velocity.

Quinidine.—Since quinidine has long been a mainstay of antiarrhythmic therapy, the clinical applications of the ectopic focus theory will be discussed with respect to this drug. High blood levels of quinidine depress excitability more than do low blood levels.[16] The importance of adequate blood levels of the drug in the treatment of clinical arrhythmias can thus be explained. High concentrations may depress excitability enough to inactivate an ectopic focus, thereby restoring normal rhythm. In the same patient, lower concentrations may have no significant effect on excitability or may depress the focus only enough to slow the rate of discharge, thereby slowing the auricular rate. The application of these principles in a typical auricular arrhythmia is shown diagrammatically in figure 6. A

Fig. 6.—Diagrammatic drawing of auricle during typical auricular arrhythmia. Each wave initiates at ectopic focus and spreads outward to encompass entire auricle. *A*, effect of small dose of quinidine. Arrows indicate quinidine-induced depression of excitability. Low concentration of quinidine depresses excitability of ectopic focus enough to slow its rate of discharge but not enough to inactivate it. Auricular rate therefore decreases while arrhythmia persists. *B*, effect of large dose of quinidine. Excitability is depressed enough to inactivate focus, thereby terminating arrhythmia. Sinus node resumes pacemaking function and normal sinus rhythm is now present.

slowing of auricular rate occurs when the excitability of the focus is moderately depressed, as represented by the small arrows in figure 6*A*. When excitability is further depressed, the focus becomes inactive and normal sinus rhythm recurs (fig. 6*B*).

Differences in the blood threshold levels of the drug in different patients may be attributed to variations in the strength of the ectopic focus. A "strong" focus is more difficult to inactivate than a "weak" focus; hence a patient with a well-established arrhythmia usually has a high blood threshold level of the drug because the ectopic focus is relatively strong. On the other hand, a patient with a paroxysmal arrhythmia usually has a low drug blood threshold level because the focus is weak. Arrhythmias that can be terminated only with extremely large amounts of quinidine often recur as soon as its blood level drops. Some patients require a concentration of 8 to 10 mg. to prevent recurrence. The ectopic focus in such instances apparently is strong enough to resume its activity despite relatively high quinidine blood levels. Since the doses required for conversion and maintenance may be dangerously large, it is usually wiser to let these arrhythmias persist. Figure 7 shows the therapeutic problem presented by a strong ectopic focus. Extremely high quinidine blood levels may temporarily inactivate the focus, thereby restoring normal rhythm (fig. 7*A*). When the blood level begins to fall, however, the focus again becomes active and the arrhythmia returns (fig. 7*B*).

Quinidine generally slows the rate of auricular arrhythmias in man whether or not it succeeds in restoring normal rhythm. If the arrhythmia continues, the auricular rate is slower than it was before the treatment. If the arrhythmia stops, a decrease in auricular rate precedes the onset of normal rhythm. Brown [16] has observed that this response to drugs is characteristic of arrhythmias resulting from an ectopic focus. Arrhythmias of the circus movement type, in contrast, were found to terminate without preliminary slowing of the rate. Moreover, circus movement arrhythmias did not recur after conversion, while ectopic focus arrhythmias reappeared when the blood level of the drug dropped. Thus, the preliminary slowing of the rate and the tendency to recurrence that characterize spontaneous arrhythmias in man are indicative of an ectopic focus rather than of a circus movement. These two clinical phenomena are readily explained by the ectopic focus theory, as shown in figures 6 and 7. The preliminary slowing of auricular rate is attributed to a progressive decrease in excitability that gradually slows the rate of discharge of waves from the focus as the quinidine blood level rises (fig. 6*A*). Normal rhythm recurs when excitability finally is depressed enough to inactivate the focus (fig. 6*B*). Subsequent recurrence of the arrhythmia represents reactivation of the focus, which recovers its excitability as the quinidine blood level declines (fig. 7*B*). One more clinical effect of quinidine to be considered is the widening of the complexes. This presumably results from a slowing of conduction velocity. Impulses travel away from the ectopic focus more slowly, thereby increasing the duration of the beat. Procaine amide, like quinidine, depresses excitability and slows conduction velocity in auricles and ventricles.[17] The foregoing comments on the antiarrhythmic action of quinidine may therefore also be applied to procaine amide.

Theoretically, drugs could stop and slow arrhythmias by lengthening the refractory period as well as by depressing the excitability of an ectopic focus.[12b] Foci can discharge impulses only during the nonrefractory period; hence the rate of discharge from an ectopic focus might decrease if the refractory period were lengthened, thereby decreasing the rate of the arrhythmia. If the rate of discharge from the focus finally dropped below the sinus rate, normal rhythm would recur. The ectopic focus

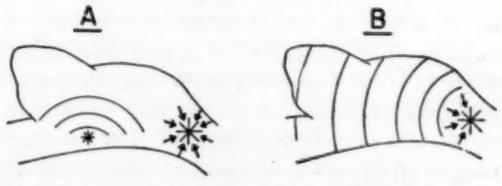

Fig. 7.—Diagrammatic drawing of auricle containing "strong" ectopic focus during treatment of arrhythmia with quinidine. *A*, quinidine inactivating ectopic focus by depressing its excitability. Flutter therefore ceases and normal rhythm resumes. *B*, quinidine blood level beginning to drop. "Strong" focus again becomes active, giving rise to recurrence of arrhythmia.

theory thus can relate the antiarrhythmic effects of drugs either to a lengthening of the refractory period or to a depression of excitability. In view of the available pharmacological data, depression of excitability appears to be the most probable explanation at the present time. Nevertheless, the nature of an ectopic focus in the human heart and its response to drugs has not yet been demonstrated by direct methods. It is possible that subsequent studies of these problems will establish a relationship between clinical changes and changes in the refractory period in patients receiving arrhythmic therapy.

Our experience is that the ectopic focus theory of antiarrhythmic drug action makes treatment more rational and more interesting. It is of practical value in estimating proper dosage for a given patient and in judging whether to attempt conversion. It explains why the outcome of therapy is sometimes successful and sometimes disappointing. It accounts for the various clinical effects of antiarrhythmic agents, including changes in rate and recurrence, and it is consistent with present pharmacological knowledge. It is easily understood by students and clinicians. Finally, it is in accordance with the previously discussed evidence that spontaneous arrhythmias in man may result from a rapidly discharging ectopic focus rather than from a circus movement.

SUMMARY AND CONCLUSIONS

The mechanism of auricular fibrillation as it occurs in man can be determined by studying the exposed fibrillating auricles of patients. Direct leads and high-speed color motion pictures were therefore recorded of the auricles of 15 patients with spontaneous auricular fibrillation before mitral commissurotomy. These direct methods of observation revealed a chaotic disturbance of auricular activity unlike anything seen during other arrhythmias. The fibrillation consisted of heterorhythmic large and small waves occurring simultaneously at rapid and irregular rates. No circus movement was found in the fibrillating auricles of the 15 patients.

A comparison is made between auricular fibrillation, flutter, tachycardia, extrasystoles, and normal sinus rhythm in man. In normal rhythm as well as in all auricular arrhythmias except fibrillation, electrical and mechanical waves pursue an orderly course from their site of origin to the extremities of the auricles. Auricular fibrillation represents a complete breakdown of this orderly activity. The nature of depolarization and contraction in the fibrillating auricles is entirely different than in normal rhythm or the slower arrhythmias.

Auricular fibrillation in man usually begins with an episode of flutter or with a single extrasystole. If the fibrillation is preceded by flutter, it may be attributed to a breakdown of orderly activity occurring when an ectopic focus discharges impulses so rapidly that the auricle cannot respond in a coordinated manner. The rate at which this breakdown occurs is termed the "fibrillation threshold." Fibrillation may begin after an extrasystole if the auricles are already disturbed and irritable, as in old persons and in those with hyperthyroidism, heart failure or abnormal neurogenic tone. In these instances, the extrasystole falling during the vulnerable period of the cardiac cycle presumably precipitates a complete breakdown of orderly activity. The frequent occurrence of unexplained fibrillation in old persons suggests that the tendency to maintain orderly auricular activity may diminish with age. Auricular fibrillation thus develops readily in elderly patients without organic heart disease or other specific etiological conditions while it rarely occurs in young persons even in the presence of profibrillary factors.

Although auricular fibrillation usually occurs in the presence of organic heart disease, it is also a frequent complication of functional disorders, such as thyrotoxicosis or abnormal neurogenic tone. These diverse conditions may give rise to different types of auricular ectopic foci, each of which is capable of producing fibrillation. It appears improbable that the wide variety of profibrillary disorders could all initiate self-perpetuating circus movements that require a specific combination of circumstances relating to the condition of the myocardium, the length of the circus pathway, the refractory period, the conduction velocity, and daughter waves.

A rapidly discharging ectopic focus is essential to the perpetuation of auricular fibrillation, at least in some patients. Quinidine gradually slows the rate of discharge from the focus, thereby reversing the process of breakdown that characterizes the onset of fibrillation. Orderly flutter waves replace the disorganized fibrillary activity as the rate drops below the fibrillation threshold. Normal sinus rhythm recurs when the focus finally becomes inactive. This sequence of events can be observed in most patients during the quinidine-induced termination of fibrillation if electrocardiograms are recorded at frequent intervals. Recent clinical and pharmacological observations appear incompatible with the theory that antiarrhythmic drugs close the excitable gap on a circus pathway. It seems more likely that drugs stop or slow auricular arrhythmias by depressing an ectopic focus. Normal rhythms recur if the focus is inactivated. A slowing of auricular rate results if the rate of discharge from the focus is decreased. Quinidine and procaine amide seem to depress ectopic foci by raising the threshold of excitability or by lengthening the refractory period. This theory may also be applicable to arrhythmias of ventricular origin. Antiarrhythmic drug action in man may be explained more simply, more rationally, and more consistently by the ectopic focus theory than by the circus movement theory.

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The Pathologic Picture of Infection.—The changing pathologic picture of infection of the past few years presents a striking contrast to that seen before the introduction of chemotherapy and antibiotic treatment. In fact some frequently lethal diseases which were treated so ineffectually prior to 1940 have now become essentially nonlethal, and their virtual elimination as a cause of death has materially modified the practice of pathology. As lobar pneumonia, purulent meningitis, mastoiditis, puerperal sepsis, septicopyemia, venereal disease and others have gradually vanished from the necropsy room, life in the morgue has become correspondingly placid. . . . Changing pathologic patterns of infection have become evident so recently that it is not to be wondered at that the incidental problems associated with the use of the chemotherapeutic and antibiotic agents seem at times to overshadow the significance of the overall accomplishments. Nevertheless, the special problems of antibiotic resistance of microbic strains, of superinfection, and of drug reactions should be constantly balanced against the facts of declining death rates and decreasing morbidity. . . . The man-made diseases will presumably be with us so long as chemists continue to manifest their remarkable resourcefulness in providing new compounds for clinical use. In the meantime pathologists will also have as one of their duties the study of the effects of these compounds upon living tissues.—P. R. Cannon, M.D., The Changing Pathologic Picture of Infection Since the Introduction of Chemotherapy and Antibiotics, *Bulletin of the New York Academy of Medicine*, February, 1955.

LOCALIZATION OF INTRACRANIAL LESIONS BY SCANNING WITH POSITRON-EMITTING ARSENIC

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and
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Moore[1] first reported in 1948 his pioneer efforts to localize brain tumors by external counting of the gamma radiation from diiodofluorescein labeled with iodine 131. The method consists of intravenous injection of the radioactive substance and subsequent measurement of gamma radiation emerging from the head by means of a suitable detector placed at various positions on the scalp. The presence of a tumor is indicated by a reading of asymmetrical activity or by divergence from a pattern of normal observations. At the same time, Selverstone and Solomon[2] were demonstrating that the beta emitter phosphorus 32 injected as the phosphate would also localize in brain tumors. The localization and demonstration of these lesions by a probe counter during operation has since become an accurate, routine procedure with us.[3] The precision of the method has been shown in postmortem material by Selverstone and White.[4] A useful technique for localization of the increased gamma radiation arising from the tumor has presented more problems. Although Ashkenazy[5] in 1951 reported 92% accuracy in his series, most workers obtained much poorer results. For example, in their studies, Belcher and co-authors[6] localized with I^{131}-labeled diiodofluorescein only 1 of 20 subsequently verified tumors. The use of radioactive iodinated human serum albumin (RIHSA)[7] has yielded more protractedly useful differential counting rates over the tumor. Peyton and co-workers[8] localized in this way 70% of tumors, and Dunbar and Ray[9] have recently localized correctly 61% of 41 brain tumors by this method.

COINCIDENCE COUNTING OF PHOTONS

A disadvantage of the use of gamma-ray-emitting isotopes for localization is the scatter of these rays within the head and the practical difficulty of excluding rays entering the detector at an angle. As a consequence, the photons arising from a small area in the brain are dispersed over a wide area at the surface of the head. There is, however, a special kind of paired electromagnetic radiation in the range of ordinary gamma rays that arises when a positron and an electron collide and undergo "annihilation." This process occurs following the slowing down of the positron, usually within about a millimeter of the site of positron emission. The mass of the positron-electron pair appears as kinetic energy of two electromagnetic quanta, which leave the scene of the annihilation back to back, that is, at an angle to each other of 180 degrees. If a pair of scintillation counters is placed on either side of the source of such radiation, electrical circuits associated with the counters can be so arranged that no count is recorded unless each photon of the annihilation radiation pair strikes its detector. If one ray interacts with matter on the way and is scattered, no count occurs. The tactic of recording only the counts occurring simultaneously constitutes a so-called coincidence counting system. Figure 1 illustrates these points. In addition to the elimination of scattered radiation, a high degree of resolution may be obtained with this method, and the sensitivity distribution is symmetrical from one side of the head to the other.

Advantages of Coincidence Counting.—The striking advantage of such a system for giving precise information as to the size and shape of a source of radioactivity is indicated in figure 2. In figure 2*A*, six small tubes are arranged in the shape of an X, as indicated by the six cylinders enclosed by continuous lines, and contain a gamma-ray-emitting isotope. A scintillation counter 13 cm. away is passed slowly and continuously from top to bottom and side to side to scan the whole area. This simulates the situation in which such a distribution of radioactivity lies in the midsagittal plane of the intracranial cavity and the detector is moving parallel to that plane at the surface of the scalp. The locus and density of the gamma radiation is indicated by the disposition of the small, rectangular stamp marks. With perfect collimation and elimination of scatter, all stamp marks would overlie the tubes. That this is not the case is obvious. In figure 2*B*, the tubes contain a positron emitter, and coincidence counting of the paired annihilation

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This study was done with the support of the Atomic Energy Commission, an institutional grant from the American Cancer Society to the Massachusetts General Hospital, the Neuro-Research Foundation, and an anonymous donor to Dr. James C. White.

Patients of Drs. James C. White, H. Thomas Ballantine Jr., Louis Bakay, John Drew, William James, Jost J. Michelsen, and others on the neurological service of Dr. Raymond D. Adams were studied.

1. Moore, G. E.: The Use of Radioactive Diiodofluorescein in the Diagnosis and Localization of Brain Tumors, Science **107**: 569-571 (May) 1948.

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8. Peyton, W. T.; Moore, G. E.; French, L. A., and Chou, S. N.: Localization of Intracranial Lesions with Radioactive Isotopes, J. Neurosurg. **9**: 432-442 (Sept.) 1952.

9. Dunbar, H. S., and Ray, B. S.: Localization of Brain Tumors and Other Intracranial Lesions with Radioactive Iodinated Human Serum Albumin, Surg., Gynec. & Obst. **98**: 433-436 (April) 1954.

gamma rays is occurring while both detector heads move together, one on either side of the array. The resolution is improved to a point where the outline of the tube is visible and the nodes between the ends of the tubes are apparent.

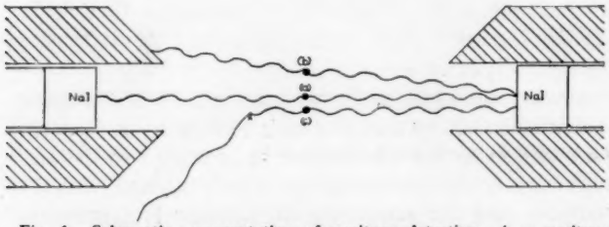

Fig. 1.—Schematic representation of positron detection. *A*, a positron annihilation producing two annihilation quanta which enter the two detectors and result in a coincidence count; *B*, the case where one quanta is detected and the other not, resulting in no coincidence count; *C*, two annihilation quanta which would normally produce a coincidence count but, because of a scattering interaction of one, do not.

The value of the positron method was presented by one of us (W. H. S.)[10] and by Wrenn and co-workers [11] in 1951. The additional advantages of using an automatic, continuous scanning technique became apparent in 1952, at which time Brownell designed the apparatus to achieve this.[12] Figure 3 illustrates the type of data obtained when the pairs of detector tubes are set by hand at each of 53 points in the sagittal plane alongside the head. The number of coincidence counts at each point following the intravenous injection of arsenic 74 is indicated in the appropriate square. In the five squares over the anterior temporal region, the counts were much higher than most, ranging from 71 to 85. In a posterior frontal and in a superior occipital square, the counts were 74 and 83 respectively. Whether these two isolated high counts indicated other tumors in addition to the main temporal lesion was questionable. At postmortem examination (no operation was performed) a glioblastoma was found confined to the temporal lobe. In this method the labor of recording the data and the difficulty in its interpretation are greater than in the method to be described.

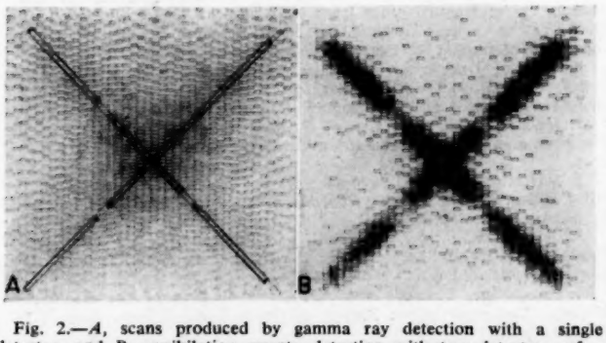

Fig. 2.—*A*, scans produced by gamma ray detection with a single detector, and *B*, annihilation quanta detection with two detectors, of a phantom consisting of fine tubes filled with a radioactive solution. The extent of the solution is indicated by the heavy lines in *A*. The increased resolution with positron annihilation detection is obvious. The length of the symbol in these scans is 0.5 cm., whereas in routine scanning a 1 cm. symbol is used. The aperture in the shielding was 1 in. (2.5 cm.) in diameter.

10. Sweet, W. H.: Uses of Nuclear Disintegration in the Diagnosis and Treatment of Brain Tumors, New England J. Med. **245**: 875-878 (Dec. 6) 1951.

11. Wrenn, F. R., Jr.; Good, M. L., and Handler, P.: The Use of Positron-Emitting Radioisotopes for the Localization of Brain Tumors, Science **113**: 525-527 (May 4) 1951.

12. Brownell, G. L., and Sweet, W. H.: Localization of Brain Tumors with Positron Emitters, Nucleonics **11**: 40-45 (Nov.) 1953.

AUTOMATIC CONTINUOUS SCAN

Positrocephalogram.—In the technique as evolved, motors move the paired scintillation detectors slowly, replacing stationary counts. Each time a given number of coincidence counts (now 10) is recorded, a stamp mark is made on a sheet of paper by equipment on an arm that moves in 1:1 ratio with relation to the head. The addition of a carefully drawn outline of the head on the sheet gives, in the normal subject, the type of record seen in figure 4. This scan one hour after the intravenous injection of As^{74} reveals a denser concentration of coincidence counts around the periphery than over the center of the cranial vault, as well as a denser concentration in the face, below the line from the posterior margin of the orbit to the tragus of the ear. In studies one day after injection of As^{74} these areas of increased concentration are much less pronounced (fig. 5). This type of scan, which we have called a positrocephalogram, will locate accurately in the sagittal plane a small area of increased radioactivity but gives no information as to the side or degree of lateralization of this area:

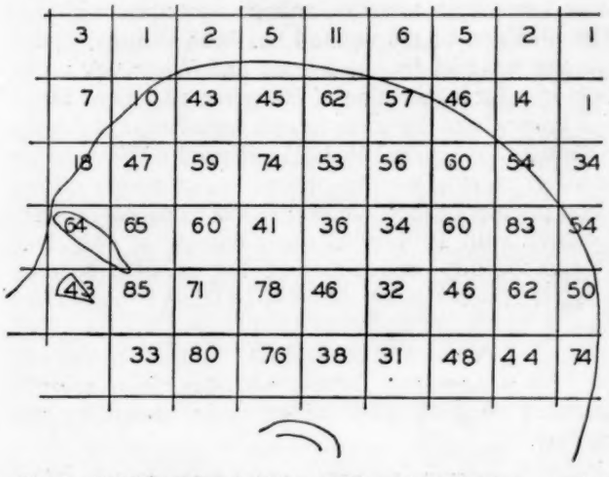

Fig. 3.—Point-by-point coincidence counting of arsenic 74 in a patient with left temporal glioblastoma.

Asymmetrogammagram.—Such data are yielded by another type of recording of the total of the information arriving at both detector heads. The nearer the source of high activity to one detector, the higher will be the total gamma count there as compared with the other one, because of the inverse square effect of increasing distance. The degree of asymmetry of the total gamma count on the two sides of the head is recorded automatically as an asymmetrogammagram, in the following fashion. Each pulse recorded by the right detector is presented to a condenser as a positive pulse and each originating from the left detector, as a negative pulse. If the two detectors receive identical numbers of pulses, the charge and voltage on the condenser remain zero. If the right detector receives more radiation, the condenser will charge positively until it reaches a preset voltage, at which time it causes a curved mark to be made on the asymmetrogammagram and the condenser voltage returns to zero. A left imbalance produces a negative condenser voltage, causing a straight mark to be printed. If the two sides of the head contain symmetrical amounts of radia-

tion, no stamp marks should appear at all. In practice, we usually see even in normal subjects a few more marks of asymmetry than in figure 6.

The two scans, the positrocephalogram and the asymmetrogammagram, are recorded simultaneously. The time required for scanning of the entire head is one hour, during which the patient lies comfortably supine with

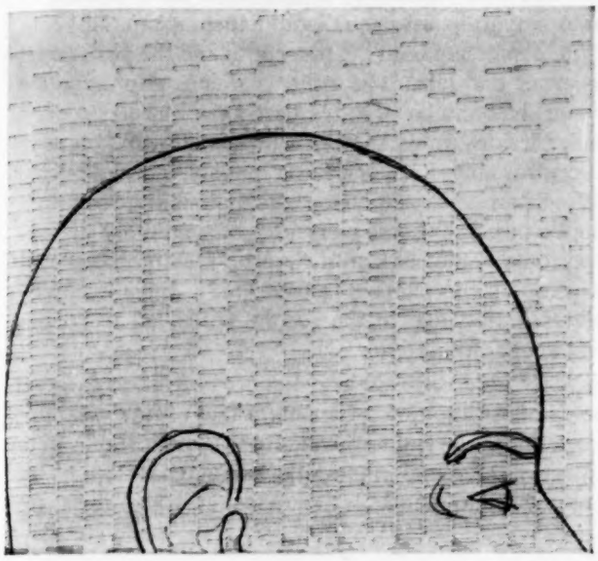

Fig. 4.—Positrocephalogram made one hour after injection of arsenic 74 in a normal subject.

the head gently fixed in position. The procedure is carried out within one or a few hours after the injection and is usually repeated without additional injection of isotope the following day.

RADIOACTIVE ISOTOPES

Choice of Isotope.—The ideal isotope would be easily produced and have a convenient half-life of at least several days, a high percentage of positron emission, a lack of extraneous gamma radiation, and a marked tendency to concentrate in neoplasms as opposed to normal cerebrum and muscle. The positron emitters copper 64, manganese 52, arsenic 74, and rubidium 84 were all tested in gliomas and cerebrums of mice [13] and all yielded useful tumor-to-brain ratios. Cu^{64}, the only feasible reactor-produced positron emitter, has the inconvenient half-life of 12.8 hours. Mn^{52} was so easily produced in the cyclotron from naturally occurring chromium that it was tried out in man. However, in addition to its positrons, it has highly energetic gamma radiation up to 1.46 mev. These rays from the body penetrated even heavy lead shielding above the shoulders and produced so many spurious coincidences that Mn^{52} was abandoned. Vanadium 48 presented the same problem. Rb^{84} has as a target material the gas krypton; hence, it is difficult to produce in useful quantity. Thus we were left on purely physical grounds with As^{74}, which, fortunately, works.

Method of Preparation and Administration of Isotopes.—As^{74} is produced by the deuteron bombardment of germanium and is separated by the method of Irvine and Backofen [14]: 1 mg. of arsenic as sodium arsenate (Na_3AsO_4) is added as carrier for about 12 mc. of As^{74}. Significant quantities of As^{72} (26 hour half-life) are produced and are used immediately following separation. The material is diluted to 50 cc., filtered, and sterilized in sealed glass bottles. The usual dose is 1.5 mc. of As^{74} to a 70 kg. (154 lb.) adult. This contains a maximum of 0.2 mg. of metallic arsenic, whereas a common daily dose of potassium arsenate (Fowler's solution) contains 7 mg. of arsenic.

Ratios of Concentrations in Tumor, Muscle, and Brain.—On the crucial biological behavior of As^{74} with respect to ratios of concentration in tumor, muscle, and brain, we have data from both biopsy and autopsy material as well as from continuous probe counting in vivo. We have also studied the biological half-life of the arsenate in the entire body and in various organs. This work, done in collaboration with Locksley, Aronow, and Powsner, will be presented elsewhere.

RESULTS

We are reporting on 216 patients in whom the final diagnosis is reasonably certain, out of a total of over 250 studied. The patients with space-taking lesions that we have studied with our automatic technique using As^{74} include 123 patients with verified intracranial tumors, 6 with abscesses, 1 with cysticercosis of the fourth ventricle, 1 with a subfrontal mucocele, and 3 with subdural hematomas.

The startling clarity with which the lesions may be displayed is illustrated in figure 7. The positrocephalogram shows a dense upper central concentration of activity, and the asymmetrogammagram shows an extreme right-sided asymmetry. We removed a mushroom-shaped

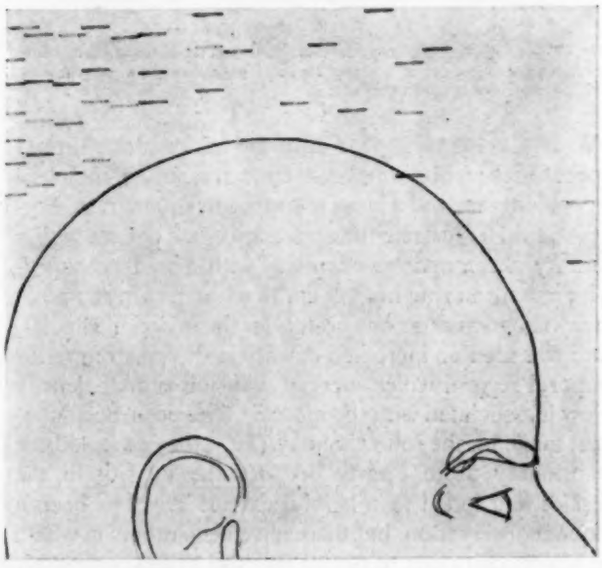

Fig. 6.—Asymmetrogammagram made one hour after injection of arsenic 74 in a normal subject.

meningioma that overlaid the right central convexity. The diameter of the tumor was as shown on the positrocephalogram; it did not have the larger dimension of the asymmetry on the asymmetrogammagram.

13. Locksley, H.; Sweet, W. H.; Powsner, H., and LePoire, J.: To be published.

14. Irvine, J. W., and Backofen, E.: Report on Separation of Arsenic, to be published.

In figure 8 is seen in the positrocephalogram a similar, although less intense, concentration in the central region, and in the asymmetrogammagram the right-sided asymmetry is less marked than in figure 7*B*. This is the typical appearance in the scans of a subcortical glioblastoma multiforme, the diagnosis made at operation in this patient.

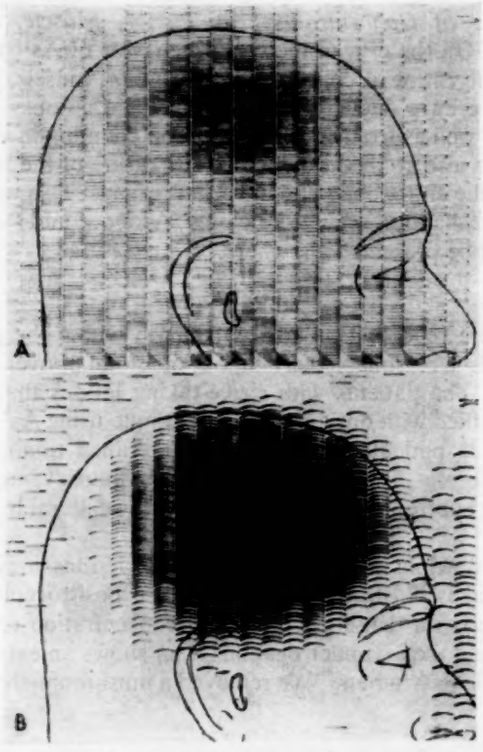

Fig. 7.—*A*, positrocephalogram, and *B*, asymmetrogammagram made one day after injection of arsenic 74 in a patient with a meningioma overlying the right central convexity.

When the tumor is near or at the midline, one should expect to see an abnormal concentration only in the positrocephalogram and a clear asymmetrogammagram. Figures 9 and 10 illustrate the appearance in a patient with a pituitary chromophobe adenoma with a midline suprasellar extension roughly 1.5 cm in diameter. In the positrocephalogram done one hour after the injection (fig. 9), there was seen an increased density in the upper anterior temporal region, which merged with the similar density below it associated with the muscles. The positrocephalogram made on the following day (fig. 10*A*) revealed the abnormality more clearly because the density in the muscles had faded to a helpful extent. This has been a frequent observation, but there have been others in which the abnormality due to tumor has also faded completely on the first postinjection day, so that the late scan was of no use. In still others consistent, though slight, abnormalities on both days led us to positive diagnosis we should not otherwise have ventured. The asymmetrogammagram made the day after injection (fig. 10*B*) shows no lateralization at the tumor site. The asymmetry to the right is not significant because it overlies the face.

15. Benda, P.; David, M., and Constans, J.: Arsenic radio-Actif ^{76}As et détection preopératoire des tumeurs cérébrales, Rev. neurol. 89: 101-109, 1953.

The method has proved sufficiently sensitive to yield clear-cut positive results in two patients in whom both arteriography and pneumoencephalography had recently failed despite technically useful filling. The positrocephalogram of one of these (fig. 11) shows a definite central parasagittal lesion that in the asymmetrogammagram is seen to be left-sided. This patient's focal seizures, beginning in her right arm, proved at craniotomy to be associated with a meningioma of about 25 gm. depressing both the precentral and the postcentral gyri near the falx. The other patient, also a young woman, had similar seizures that were due to an even smaller lesion, unfortunately a metastatic carcinoma in the central sulcus. In the latter patient, normal scans, arteriograms, and pneumoencephalograms were followed within a month by some worsening of symptoms. She refused to have the surgical diagnostic measures repeated but accepted the painless isotope study, and the abnormal result obtained in the second study led us to immediate operation.

The tactic can also aid in avoidance of fruitless surgery. The demonstration of two or more foci of increased uptake of As^{74}, especially when there was clinical reason to suspect intracranial metastatic tumor, has led us to recommend no surgical treatment in some instances (fig. 12).

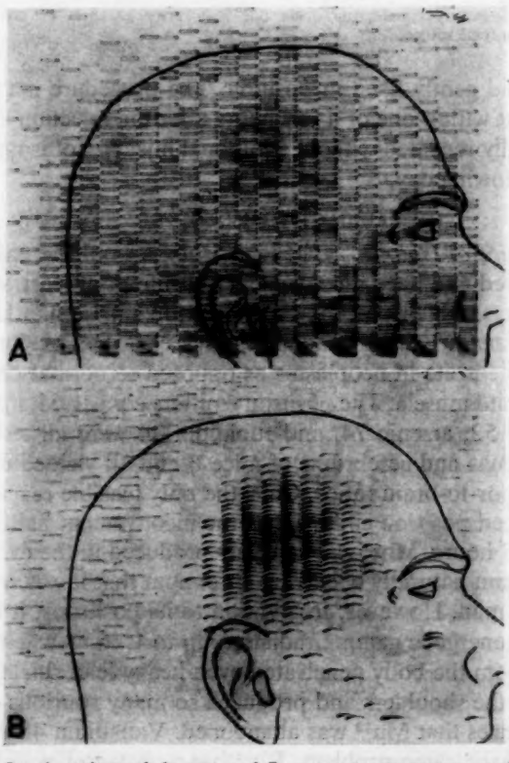

Fig. 8.—*A*, positrocephalogram, and *B*, asymmetrogammagram made one day after injection of arsenic 74 in a patient with a subcortical glioblastoma multiforme.

Intracranial Neoplasms.—Our data on patients with neoplasms are summarized in the table. The scans were diagnosed without reference to clinical facts for the purpose of this tabulation and were classified as either normal or abnormal. Our best results occurred in cases of meningioma, which usually takes up much larger amounts

of the arsenate than does the normal brain. Benda and coauthors [15] made similar observations on three meningiomas in patients to whom As^{76} had been given as the arsenate. The only one we missed out of 24 studied was a 6 gm. lesion arising from the tuberculum sellae. Of the glio-

Results of Positron Scans of Patients with Diagnosed Intracranial Lesions

Lesion	Abnormal Isotopic Concentration	No Abnormal Isotopic Concentration
Neoplasms		
Glioma	10	4
Astrocytoma		
Ependymoma	2	0
Glioblastoma	38	4
Oligodendroglioma	0	2
Brain stem (no biopsy)	1	3
Carcinoma, metastatic	9	4
Meningioma	23	1
Melanoma	2	1
Neuroma, acoustic	0	3
Chromophobe adenoma	4	2
Craniopharyngioma	2	4
Pinealoma	0	1
Tumor in 3rd ventricle	0	1
Type undetermined	2	0
Total	93	30
Abscesses or Cysts		
Supratentorial abscess	5	0
Cerebellar abscess	0	1
Cysticerosis, 4th ventricle	0	1
Subfrontal mucocele	1	0
Total	6	2
Disorders of Blood Vessels of Brain		
Thrombosis or hemorrhage	3	15
Arteriovenous malformation	1	4
Subdural hematoma	2	2
Subarachnoid hemorrhage and/or aneurysm	1	3
Total	7	24

blastomas, we missed 4 of 42. Two of these contained large cysts of 30 and 40 cc. volume respectively. The cystic fluid often holds even less radioactive isotope than the normal brain and hence would tend to cancel out the higher concentration in the adjoining tumor. In the other

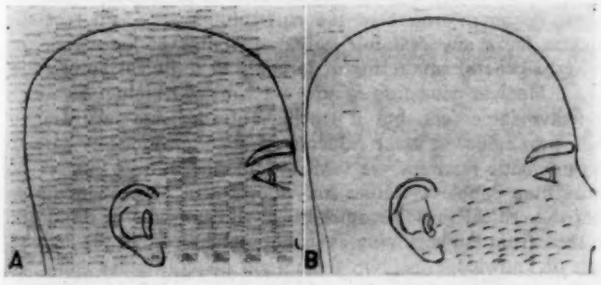

Fig. 10.—*A*, positrocephalogram, and *B*, asymmetrogammagram made one day after injection of arsenic 74 in a patient with a pituitary chromophobe adenoma with a midline suprasellar extension.

two cases of glioblastoma, we were suspicious of abnormal concentration in the neoplastic area but did not make a definite diagnosis. We missed the diagnosis in 4 of 13 studies of patients with metastatic carcinomas. To one of these cases, in which an error was made the first time and corrected a month later, we have already referred. Two of the remaining three patients had small tumors in a cerebral hemisphere; the fourth had a larger, 3 cm., tumor within the cerebellar hemisphere at the cerebellopontine angle. The percentage of missed diagnoses becomes higher among cases of the slower-growing avascular gliomas and those invading the brain stem. Of course, a small amount of neoplasm is responsible for major signs

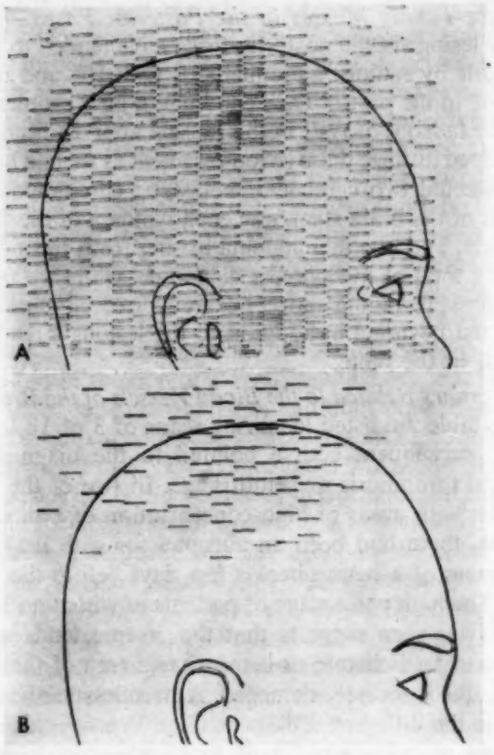

Fig. 11.—*A*, positrocephalogram, and *B*, asymmetrogammagram made one day after injection of arsenic 74 in a patient with a meningioma at the precentral and postcentral gyri near the falx on the left side.

in the latter group. We also did poorly in instances of neoplasm in and about the sellar area and third ventricle; we did not detect a single acoustic neuroma. Our diagnostic accuracy of 93 correct out of 123 neoplasms, or 75%, may fall rather than rise despite improvements in the method because the simplicity and painlessness of the procedure lead to its use in the presence of slight symptoms, before a pneumoencephalogram or arteriogram would be tried. Tumors in many such patients who are seen early are going to escape us on the first or second examination. A major advantage to the surgeon is the delineation of essentially the full extent of the tumor, so that he can plan his exposure properly. In the latter half of the series, we acquired such confidence in the data that in many of the patients we operated without previous radiography of the arteries or ventricles.

Intracranial Abscess or Cyst.—Our small experience with intracranial abscesses and cysts is summarized in the table. Each of the abscesses in a cerebral hemisphere was detected. The high intracranial pressure and precarious state of many patients with brain abscess give ventriculography a special hazard, the more so since the abscess

may rupture into the ventricle during the procedure. Our scans in patients with cerebral abscess have been so clear-cut that we do not now resort to air studies in such dangerously ill patients when the scans give corroboration of the clinical localization (fig. 13). The lone cerebellar abscess we missed. We should not have expected the Cysticercus cysts in the fourth ventricle to take up large amounts of arsenic; they too, at least in the posterior fossa, will probably continue to escape determination by this method.

Space-Taking Masses in the Posterior Fossa.—Neoplastic lesions in the posterior fossa have tended to elude diagnosis by radioisotopic methods with I^{131} and potassium 42 in the past.[16] They continue to be a problem for us. The fadeout of As^{74} in the muscle after 24 hours has not helped localize these lesions as much as we had hoped. We detected two cerebellar metastatic carcinomas, one glioma of the brain stem, one ependymoma of the fourth ventricle, and one meningioma arising from the sigmoid sinus, a total of five correct diagnoses, while we missed 10 lesions, including another cerebellar carcinoma and a cystic astrocytoma in addition to the lesions already indicated in the table.

Disorders Related to the Blood Vessels of the Brain.—In the table are listed localizing scans of 3 of 18 lesions whose subsequent course pointed to the diagnosis of cerebral thrombosis or hemorrhage. In two of the three patients with areas of high concentration of radioactive arsenic, there had been an abrupt ictus with major involvement of a hemisphere a few days before the scanning. The high percentage of patients in whom no localization was seen suggests that the arsenic tends not to pour into an ischemic or hemorrhagic area of the brain unless this is severely damaged. A harmless method that will aid the differential diagnosis between neoplasm and cerebral vascular accident is highly desirable, and we trust this type of scan may evolve into such a method. Its need has been emphasized by the observation of older patients in whom marked improvement in cerebral signs and symptoms obscured the realization that a tumor was present.

Arteriovenous malformations did not take up much radioactive arsenic in four of five cases. In a patient with a massive parietal lesion and one of four patients with a berry aneurysm and subarachnoid hemorrhage a scan was abnormal shortly after an ictus with bleeding. Of our four patients with subdural hematomas, we saw no abnormal distribution of As^{74} in two. Here, again, the brain damage by compression from the adjoining hematoma may perhaps exclude this substance. Dunbar and Ray,[9] however, saw striking pictures of increased uptake of radioactive iodinated human serum albumin in the brains of their four patients with largely unilateral hematomas, and Peyton and others[8] had another such case.

Other Disorders.—In 55 other patients scanned, the diagnoses covered a full range of the remaining diseases in which one might suspect intracranial tumor or abscess. In three of these, the scans appear to have led us wrongly to sustain the suspicion of a mass lesion. This occurred in 2 of 20 patients with seizures; in one of these the scan was done shortly after a burst of focal seizures with postictal paralysis. A breakdown of the blood-brain barrier seems to have occurred in the discharging cortex. Peyton and co-authors[8] record a similar experience. The other error was in a patient who had dilated ventricles associated with adhesions at the foramen of Magendie. In this miscellaneous group, we have then an accuracy of normal scans of 93%.

FUTURE PLANS

An improved model of the apparatus is about to go into operation. Its detectors have a decreased aperture and a larger counting crystal, with which we have evidence that we will obtain sharper pictures. Provision for scanning in the long axis of the head has also been made.[16a] This apparatus is obtainable from the Atomic Instrument Company, 84 Massachusetts Ave., Cambridge, Mass.

SUMMARY

By a technique for automatic scanning of the head after intravenous injection of positron-emitting arsenic 74 as sodium salt, two types of data are recorded simultaneously in records that we have called a positrocephalogram and an asymmetrogammagram. The advantages are: 1. It is harmless, painless, and simple. 2. The data automatically evolve pictorially, so that their preparation and interpretation require only a few minutes. 3. The localization in the sagittal plane is more precise than that obtainable when total gamma radiation only is counted. It guides the surgeon well for his exposure, eliminating the need for arteriography or pneumoencephalography in a growing number of cases. 4. Accuracy is now about 75% for tumors and 83% for abscesses. Only 17% of patients with cerebral thrombosis or hemorrhage had abnormal scans.

Massachusetts General Hospital (Dr. Sweet).

16. (*a*) Selverstone, B.; Sweet, W. H., and Ireton, R. J.: Radioactive Potassium, a New Isotope for Brain Tumor Localization, S. Forum (1950) 371-375, 1951. (*b*) Dunbar and Ray.[9] (*c*) Peyton and others.[8]

Medical Education.—Medical Schools have become technical institutes, and this is the most significant of the few changes that have crept into medical training in the last three decades. The sooner that this fact is openly acknowledged, and the pretence that Medical Schools can provide a University education is dropped, the easier will become the task of those who set themselves up as reformers of the curriculum. . . . In fact the student lacks any real intellectual discipline and, instead, acquires a general smattering of jargon and technical knowledge. . . . Medical education is now a technical training. So much is unavoidable fact, but if teachers of medicine regard it as their prime duty to make students examination-proof by spreading dogmatic finalities, we shall become, as Billroth feared, no more than cobblers. Rather may the student be brought up so that the critical spirit becomes his natural attitude of mind and so that, from the beginning, he is not marshaled into the acquisition of knowledge, neither are he and his colleagues subjected to the processes of levelling which are the inevitable result of mass lectures and instruction. . . . May the student be given opportunity and encouragement to develop for himself a discipline and an independence of thought, which he may retain long after the official medical curriculum is completed, so that he may preserve the proper attitude of a student throughout the time that he is engaged in the practice of medicine.—G. Hatcher, M.D., Some Thoughts on Medical Education, *Middlesex Hospital Journal*, December, 1954.

THERAPEUTIC USE OF COLD

William Bierman, M.D., New York

The term cold refers to the abstraction of heat, to the substance by means of which such abstraction is effected, and to the sensation created by such abstraction. The sensation of cold is evoked when the temperature of the substance is lower than that of the body area to which it is applied. It is possible to develop the paradoxical situation in which the same substance will feel cold to one hand and warm to the other when one hand has been previously immersed in warm water and the other in cold water. The temperature of the skin surface of the torso can be regarded as the neutral point and is usually about 93 F (33.9 C). When water is used as a therapeutic agent it is called tepid if its temperature is between 80 and 93 F (26.7 and 33.9 C); cool, between 65 and 80 F (18.3 and 26.7 C); cold, 55 and 65 F (12.8 and 18.3 C); and very cold, below 55 F (12.8 C).

The substances used for the therapeutic application of cold may occur in the three forms of matter: solid, liquid, or gaseous. Examples of the solid form are ice and carbon dioxide snow; of liquid, water; of gaseous, those substances that abstract heat as they evaporate, such as, ethyl chloride, alcohol, and ether. An ice bag applied to the calf of a person can lower the temperature of the skin 41 degrees (F), that of the subcutaneous tissue 24 degrees, and the temperature of the deep muscle mass 19 degrees. Cold air can produce a fall of 11 degrees in the calf muscle. Cold water circulating through metallic applicators inserted into the rectum or vagina will produce a substantial lowering of pelvic temperatures. It is possible to reduce intracranial temperatures by ice bags applied to the forehead.[1] Ethyl chloride sprayed on the skin of the calf of a person, so as to avoid frosting, can reduce the temperature of the skin 50 degrees and that of the deeply situated muscle 7 degrees. The reduction of intramuscular temperature occurs several minutes after the lowering of surface temperature and lasts for two hours and longer after the application of ethyl chloride.[2] Wakim and his co-workers observed that ice packs applied to the knee joints of dogs markedly reduced the intra-articular temperature and the temperature of the adjacent structures.[3] This is in accord with my findings after spraying ethyl chloride over the knee joints of human beings and contrary to the reports of Hollander and Horvath.[4]

REACTIONS FROM COLD

Lewis[5] has described the reactions produced by cold as: direct and persistent response of the superficial vessels; immediate general but transient vasoconstriction by reflex action through the central nervous system; and the lowering of the temperature of the blood in the general circulation by the cool venous blood returning from the exposed areas. As cooling continues, the temperature of the limb falls. At 50 F (10 C) or lower, the skin is benumbed, fine touch sensitivity is diminished, and the muscles of the limb are less efficient. He has observed that two reactions appear after the local cooling of the skin below 32 F (0 C) for short periods of time. Freezing may take place if moisture is present; otherwise, the skin may be supercooled to temperatures as low as 5 F (–15 C). Wheals develop after either reaction. Skin that has been frozen becomes red and tender for several days, and in time, desquamation and pigmentation occur. These reactions to tissue injury are related in part to the release of histamine-like substances.

As with the local application of heat, that of cold produced changes in distant parts of the body but in the reverse order. Thus, the immersion of a person's hand and forearm in cold water will produce a lowering of the skin temperature of the toe when the peripheral circulation is normal. The failure to cause such distant changes is indicative of a compromised peripheral circulation. Cold water applied in this way can, therefore, be used as a technique for the examination of the circulation of the lower extremities in a manner comparable to the Landis-Gibbon test. The use of cold as a test for hypertension was described by Hines and Brown.[6] The hand was placed in water at 4 C for one minute, and the blood pressure was taken in the opposite arm. Readings were taken 30 to 60 seconds after immersion and until the pressure returned to the original base level. A rise in blood pressure more than 20 mm. Hg systolic and 15 mm. Hg diastolic was considered characteristic of essential hypertension.

Wolff[7] found that the vasoconstriction underlying the cold pressor response did not occur as the result of a reflex but as a response to the pain experienced during the cold immersion and that, therefore, the cold pressor test provides a measure of sensitivity to a standard painful stimulus rather than of vascular reactivity. More than 100 years ago, Esmarch,[8] who was professor of surgery at the University of Kiel, wrote: "If we look back into the history of surgery we find that by physicians of the most ancient times cold was sometimes depreciated as ineffective or dangerous. Thus Hippocrates, and after him Celsus, recommended the application of cold water to recent injuries of the most various kinds; while Galen, on the other hand, used only warm water and warm oil to wounds and, did so, probably in consequence of experiments he had made on the effects of snow and cold water upon the tissues of the body." Esmarch's book reveals that the controversy as to the relative therapeutic value of heat and cold continued from ancient to his own times.

Although a century has passed since Esmarch's review of the therapeutic uses of cold, there is still no unanimity of medical opinion as to its relative value. This is due to the necessity of relying on clinical judgment in specific instances rather than on exact objective criteria as to whether the tissue changes produced will favor healing more than they will retard it. The advisability of applying cold depends on several factors, such as the character and stage of the pathological change, the availability of other therapeutic measures, tissue reactions, and the patient's reaction. At times the determination can be made with reasonable certainty and, at others, it is made on a trial-and-error basis. Soft tissue

A condensation of this paper was read before the Section on Physical Medicine and Rehabilitation at the 103rd Annual Meeting of the American Medical Association, San Francisco, June 22, 1954.

Because of space limitations the bibliographic references have been omitted from THE JOURNAL and will appear in the author's reprints.

trauma is frequently benefited by the use of cold. Patients with contusions, strains, or sprains, if treated directly after an injury, respond with earlier motion and decreased edema if the injured area is chilled by ice, compresses, or ethyl chloride spray.[9] Application of cold is helpful for the treatment of patients with acute epididymitis. It can be used to slow the absorption of tissue fluids in patients whose allergic reactions are acute. Depending on the patient's reactions, it can prove to be more serviceable than heat in the treatment of edematous hemorrhoids, anal pruritus, and acute superficial phlebitis. Cold compresses are applied for the care of external otitis and inflammations of the eye, such as those occurring from chemical irritation as with silver nitrate. In the form of carbon dioxide snow, cold has many therapeutic applications in dermatology. Carpenter[10] lists the conditions that it can effectively treat, such as acne, angiomas, corns and callosities, verrucose eczema, keloids, lichen planus, lupus erythematosus, molluscum contagiosum, selected types of nevi psoriasis, rosacea, senile keratoses, seborrheic keratoses, tuberculosis cutis, verrucae, and xanthomas. Cold is a useful agent in dentistry. In the form of water and air it is used in the irrigation of teeth during drilling, as a diagnostic agent to test the reaction of the pulp, and for the treatment of inflammations about the mouth.

TYPES OF APPLICATION

A good technique for the application of cold is the use of ethyl chloride spray. Kraus[11] has advocated the use of ethyl chloride along with movement of the affected part in the treatment of sprains of all joints, acute and chronic muscular spasm due to low back pain, acute bursitis of the shoulder, spasm of shoulder muscles, and similar conditions. The region in which pain is produced by active motion is sprayed with the solution. The arc of the movement is gradually increased, and other painful areas are treated as they appear. The treatment lasts 10 to 30 minutes. Frostbite is prevented by the application of camphor liniment. Kraus states: "Immediate normal use of the affected part can be followed in a majority of cases, but excessive strain or sudden movement should be prohibited." If necessary, the treatment can be repeated daily and later at longer intervals.[11] I have found ethyl chloride spray to be useful for the treatment of the conditions mentioned. The technique used varies with the objectives. If reduced swelling and tissue tension, as in recent sprain of the ankle or acute shoulder bursitis, is desired, as much as 100 gm. of the solution may be applied during a period of about one-half hour in an effort to secure deep and long-lasting refrigeration. If the influence desired is essentially a reflex one, as in the treatment of muscle spasm, less solution is applied for a shorter period of time. Keeping the stream of the solution in slow but constant motion and allowing sufficiently long intervals before retreating the same area will avoid frosting.

Travell considers ethyl chloride spray as "a physical agent in a pharmacological package."[12] She has observed prompt relief of painful muscle spasms after its use and considers such relief as due to an interruption of a reversible neurogenic process responsible for maintaining pain and spasm. Such muscle spasm may be due to sudden trauma, chronic repetitive strain, or protracted chilling without abnormal neurological findings and without bone and joint pathology. The syndrome includes such disorders as: stiff neck; trismus; lumbago; sciatica; painful knees; chronic ankle pain; heel pain; tennis elbow and painful shoulder; acute sprains of the ankle, knee, wrist, or thumb; osteoarthritis of the spine or single joints; fractures; and muscle spasm secondary to acute visceral disease, such as occurs in the frozen shoulder syndrome that appears after acute myocardial infarction. Travell believes it is possible to influence the persistent somatic pain syndrome initiated by an acute visceral lesion if the acute pathological process in the viscus has ceased and the secondary myofascial trigger areas have become independent of the original source of the noxious impulses. She explained the effect of ethyl chloride spray as possibly due to an intense stimulation by the cold shock with its rapid change in skin temperature and to some degree of direct depression of the cutaneous receptors. The technique used is that of a fine jet stream that is directed to meet the body surface at an acute angle. The container is held 2 ft. away. The stream is applied in one direction, not back and forth. The sweep is started at the trigger area and is moved slowly and evenly outward over the reference zone. The optimum speed of the sweep is about 4 in. per second. Sweeps are repeated in a rhythm of a few seconds on and a few seconds off. Care is taken not to frost the skin. The muscle containing the trigger area is gently stretched. After each series of sweeps, the patient is requested to move in directions that were originally restricted and within the limits of pain. The patient is requested to perform exercises a few times daily.[12]

Using procaine infiltration of trigger areas and spraying the front of the chest with ethyl chloride, Travell reports relief of pain occurring in coronary thrombosis.[13] Based on the reports of Travell and Rinzler[14] on the effectiveness of ethyl chloride spray in blocking the somatic component of cardiac pain occurring in acute myocardial infarction, angina pectoris, and the shoulder-hand syndrome due to coronary deficiency, Stein and others[15] used the same technique to block the anginal pains that occurred after intravenous injection of ergonovine maleate that was used as a test. The possibility of influencing the pain due to gastrointestinal diseases by blocking of the trigger mechanics with the use of procaine and ethyl chloride is described by Melnick.[16]

If cold is applied locally, the temperature of a circumscribed area of the body may be maintained between 40 and 50 F (4.4 and 10 C) for several months without damage or destruction of normal tissues. However, it is dangerous to lower the temperature of the entire human body below 75 F (23.9 C).[17] A systemic temperature between 80 and 90 F (26.7 and 32.2 C) may be maintained continuously for as long as eight days.[18] As a result of the lowering of the systemic temperature, metabolism is strikingly reduced.[19] The physiological and biochemical changes include an initial rise in pulse and blood pressure preceding a gradual fall, with marked arterial and venous vasoconstriction; hemoconcentration (red blood cell count rising to 25% above normal); increase in the number of white blood cells, polymorphonuclears, and reticulocytes; decrease in sedimentation

rate and platelet count; and development of cardiac sinus arrhythmias and auricular fibrillation.[17] With diminishing temperature, the blood pressure declines and the activity phase of the cardiac cycle is prolonged. These factors, in addition to blood viscosity, reduce coronary circulation. This reduction and the depressed cellular oxidation rate weaken the myocardium. The QT segment of the electrocardiogram becomes prolonged.[20]

CHANGES DUE TO EXPOSURE TO COLD

The injuries occurring in members of the armed forces during World War II have stimulated investigations as to the changes produced by exposure to intense and prolonged cold. It was noted that prolonged immersion in cold water caused changes in the cardiovascular system, (transient auricular fibrillation and flutter, ventricular extrasystoles, prolongation of the P-R interval, and falling arterial blood pressure with narrowing of the pulse pressure); the nervous system (partial to complete loss of consciousness and irrational behavior); hemoconcentration and hyperglycemia. It is reported that as a result of experimentation on persons in concentration camps, German investigators concluded that the curve of rectal temperature of persons chilled in water 35.6 to 53.6 F (2 to 12 C) dropped slowly to 95 F (35 C) and thereafter more rapidly until death occurred at 80.6 to 78.8 F (27 to 26 C). Death was thought to result from cardiac failure. Auricular fibrillation occurred constantly when the rectal temperature dropped below 84.2 F (29 C). The blood sugar content rose in inverse proportion to the fall of the temperature. After removal of the subject from the water, the body temperature sank for 15 minutes or longer. The most effective treatment was reported to be heat applied rapidly and best administered by means of immersion in a hot bath 104 to 122 F (40 to 50 C).[21]

USES OF COLD

The possibility of lowering the temperature of the entire body was described by Currie in 1798,[22] and, in 1855, Arnott applied cold for the treatment of cancer.[23] In more recent years, Smith and Fay[24] refrigerated the human body for the treatment of cancer. They had observed that tumor cells were more readily affected by cold than were normal differentiated adult type of cells. The rectal temperature was lowered to about 80 F (26.7 C) and kept there for long periods of time up to eight days without subsequent abnormal effects. Prolonged, though temporary, periods of relief from pain occurred, although no definite regressive changes in undifferentiated cell growth were noted in deep metastatic lesions. Smith lowered temperatures of accessible tumors to 40 to 50 F (4.4 to 10 C), with regression in the size of the mass. Histologically, the tumor tissue showed degenerative changes that progressed to complete necrosis, with local disappearance of the tumor in some cases.[25] The possibility of influencing malignant disease in this manner aroused great interest, but this technique was found to be ineffective and dangerous so that it is no longer used.

Talbott and Tillotson[26] treated psychiatric disorders by means of hypothermia. They reported favorable results in young patients with schizophrenia. A less strenuous and danger-free technique to quiet manic patients is the cold sheet rung out of water at 64 F (17.8 C) and applied as a pack. For the treatment of shock due to hemorrhage or trauma, animal experimentation indicates the value of low body temperatures.[27] The fall in body temperature should be regarded not as a result of the anoxia but as a protective mechanism. It is recommended that a conscious patient be warmed or cooled in accordance with his desires and that an unconscious one requires no more external warming than a recumbent normal person.[28] Doane and Stein[9] advocate refrigeration for the care of patient with hyperpyrexia occurring after hemorrhages of various degrees, head injuries, and operations, and that of thyroid crisis and pneumonia.

The performance of cardiac surgery has been facilitated through the lowering of body temperature. Of the various techniques available for the production of hypothermia, as with immersion in cold water, placing the body in cracked ice or in a cold chamber, Bailey and his co-workers[29] prefer to use a blanket, through the coils of which fluid is circulated at a controlled temperature. This blanket is closed around the patient with a zipper. When the desired temperature, 74 to 80 F (23.3 to 26.7 C) is reached the blanket is opened but is left in place under the patient while the operation is performed. Then the cold fluid is replaced by warm water, and the patient is rewarmed to a level where respiration is spontaneous and adequate, usually at about 84 F (28.8 C). Rewarming is completed in about 12 hours. Continuous observation of the temperature is possible through the use of a rectal thermocouple. Anesthesia is considered essential for the induction of hypothermia in order to render it painless and to reduce the tendency to shivering, which retards cooling. Thiopental sodium and procaine are administered intravenously. An endotracheal tube is inserted and connected to a closed anesthesia system. A direct-writing electrocardiograph is used to detect the electrical waves associated with shivering, which indicates the need for more anesthesia. Constant observation of the electrocardiographic record is essential, since ventricle asystole or fibrillation may occur at any time of cooling. Bailey and his co-workers[29] came to the conclusions that cardiac surgery, under hypothermia, is presently of little value in acquired cardiac lesions and in lesions of the left side of the heart; that it is dangerous in adults, since the myocardium may become fatally depressed; that with the open technique it is dangerous to treat large septal defects because of the likelihood of air embolism; that the procedure is useful in small children with congenital heart disease involving the right side of the heart; and that it enhances the chance of recovery in the orthodox surgical treatment of children with cyanosis. Hypothermia permits a relatively long interruption of circulation with full recovery.

Ripstein and his associates[30] state that hypothermia is potentially of great value in cardiac surgery, because, with the decreased metabolic needs of tissues, the heart can be excluded from the circulation for prolonged periods without producing irreversible brain damage. The vena cava can be clamped, the bloodless heart opened, and surgical procedures performed under direct vision. The present-day work with hypothermia for cardiac surgery is based on the earlier studies of human refrigeration and on animal experimentations.[31] The

technique is being continuously improved, as by the use of a Satinsky clamp to occlude the outflow of the heart and to prevent air embolism with its resultant ventricular fibrillation and the use of electrical defibrillating shocks.[32] Lewis avoids coronary air embolism by outflow occlusion of the heart plus rapid filling of the left chambers of the heart with saline solution at the time of right atrial closure.[32] To facilitate the induction of the hypothermia, French investigators recommend the use of an antihistaminic drug, chlorpromazine [10-(γ-dimethylaminopropyl)-2-chlorophenothiazine hydrochloride] to inhibit the action of the thermoregulatory center.[33]

Refrigeration has been advocated for extremities that require amputation because of inadequate circulation and infection. Allen [34] summarized the advantages of this form of surgical refrigeration as: avoidance of surgical shock, control of infection and intoxication, and elimination of postoperative pain and edema. He stated that this technique permitted a reduction of local tissue metabolism, bringing it within the capacity of the impaired blood supply; poorly vitalized tissues were preserved; and clotting time was inhibited, thus minimizing the dangers of thrombosis and embolism. The advantages of refrigeration of the extremity claimed by Allen have been substantiated by some and refuted by others. Pfeiffer and coworker [35] felt that refrigeration anesthesia was the technique of choice for poor risk patients with gangrene of the extremities due to peripheral vascular disease and requiring amputation. They considered that the ease and quickness of operation and the absence of pain and of shock were advantages. Similar opinions were expressed by others.[36] Doane and Stein [9] considered they had clinically proved the value of decreasing the metabolism of severely injured extremities with refrigeration and, at the same time, causing peripheral vasodilatation by means of lumbar sympathetic block; thus, decreasing the absorption of toxins and simultaneously decreasing the spasm of blood vessels. This was done in the attempt to bring the metabolism of the extremity into keeping with the available circulation. It was the opinion of these authors that refrigeration should be used as a therapeutic and anesthetic agent for minor surgical procedures as well as in the presence of certain peripheral vascular states.

Other investigators concluded that the lowering of tissue temperatures was harmful. Muschenheim and his associates [37] observed the influence of hypothermia on experimental pneumococcic infections in rabbits. The local dermal inflammatory reaction caused by the usually nonlethal avirulent pneumococcus type 3 was reduced, but an overwhelming bacteremia developed, and death occurred. Richards [38] noted that, while refrigeration anesthesia has decided advantages in the control of shock, hemorrhage, and infections if the limb is to be sacrificed, particularly in elderly debilitated patients in toxic condition from gangrene or infection, the many advocated advantages of refrigeration in infection, shock, traumatic injuries, and vascular occlusion seem untenable. Bacterial growth can be retarded by refrigeration, but so can tissue response to inflammation, and, on the removal of the cooling, the inflammatory reaction may even be exaggerated. Large and Heinbecker found that cooling interfered with the healing of wounds [39] and that prolonged application of cold caused degeneration of nerves.[40] At the present time, refrigeration anesthesia for amputation appears to be used infrequently and only in poor risk patients with severe involvement. I have observed that this technique greatly lessened the pain in patients with prelethal thrombosis of the arteries of the lower extremities.

SUMMARY

The age-old application of cold still maintains an important place in modern medicine and has been put to new uses in treating patients with cancer, psychiatric disorders, shock, hyperpyrexia, cardiac surgery, acute epididymitis, hemorrhages, and infections.

471 Park Ave.

SPINE INJURIES

George J. Garceau, M.D., Indianapolis

Injuries to the spine include the severe fracture dislocation of the vertebrae, with paraplegia to the simple sprain of the back. Accurate diagnosis is necessary to plan the required treatment. In many instances the nature of the accident may have been so severe that the mechanics producing the injury can not be ascertained. However, if the injury was incurred with the trunk in flexion, a compression fracture may be anticipated. Such a simple act as lifting a tightly closed window has produced compression fractures of the bodies of the vertebrae. Fractures incurred with flexion may be complicated by fractures and dislocations of the pedicles, laminas, or facets. Fractures of the appendages of the vertebrae are more frequently associated with some degree of spinal cord or nerve root injury. Hyperextension fractures are rare, but, when they occur, the appendages are usually involved. An inquiry about the activity of the patient immediately after the accident will reveal valuable information about the injury to nerve tissues.

The physical examination should begin with the consideration of the position of the patient when first seen and should include bruises, contusions, lacerations, and points of tenderness. The neurological examination should include function of the limbs, reflexes, and a sensory survey. If paraplegia is present, hyperflexion of the toes or other painful stimulation will reveal information about the completeness of the paraplegia. The bladder must not be allowed to become distended. Abdominal distention may appear early, and measures for its prevention should be instituted. The patient must be moved carefully to prevent further injury to the spinal cord. Thorough x-ray examination is desirable, but the posi-

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tioning of the patient should be done with care. Anteroposterior and lateral views are necessary, and oblique views may give much information. Myelographic and spinal fluid examinations are seldom required and usually will give little information, although there are exceptions.

TREATMENT

The treatment will depend on the nature of the injury. The simple compression fracture of a thoracic or lumbar vertebra offer little difficulty. The fracture dislocation of vertebrae, with incomplete or complete paraplegia, requires an early decision as to definitive treatment, because the complications occur early, and delay may prevent recovery from the paraplegia.

Fracture Dislocation.—Neurological deficits are noted most often with the fracture dislocation type of injury. Hyperextension of the spine must be avoided, because further injury to the spinal cord may ensue from this manipulation, especially if there is some lateral displacement of the vertebrae. Open reduction is probably the safest. If simple open reduction is not possible, then resection of the facet will allow reduction. If laminectomy is done, the dura should be opened to observe the presence of a hematoma or bleeding of the spinal cord. All hematomas should be removed and hemorrhage controlled. Continued bleeding about or within the cord will cause further damage and prevent maximum recovery. Spine fusion may be done immediately or it may be delayed until the condition of the patient warrants further surgery. A plaster shell or bed is highly desirable. This shell should have a back and front piece to facilitate turning and other nursing care procedures. The patient should be on a firm bed.

Fractures of Pedicles and Laminas.—Fractures of the pedicles or laminas, without displacement, should be treated by simple immobilization in a plaster jacket. Union will usually occur in three months. Recumbency is not necessary, and the patient may be allowed to be up as soon as desired. Neurological defects associated with fractures of the pedicles or laminas and compression of the body of the vertebrae require serious consideration of open operation. Open operation is less hazardous than closed manipulation. Fragments of bone should be removed and laminectomy performed. If the neurological deficit is considerable, then the dura should be opened for thorough inspection of the cord. A plaster bed should be made for postoperative treatment.

Fractures of Transverse Process.—Fractures of the transverse processes are usually due to torsion of the spine or to great muscular strain in the patient's attempt to protect himself. As in the other fractures of the vertebrae, the surrounding soft tissues are contused and torn, resulting in hematoma formation. The safest type of treatment is immobilization in a well-fitted plaster corset, to be worn for about eight weeks. If there is only one transverse process fractured, then simple strapping of the back or a corset with stiff steel stays may suffice. If the symptoms of backache persists for months after removal of the plaster jacket, then some other reason for persistence of the symptoms must be sought. The intervertebral disks must be suspected.

Injuries to Intervertebral Disks.—Recovery from a sprain of the lumbar spine may be expected within a few weeks. If recovery does not occur in a reasonable period, then one should suspect an injury to the intervertebral disk. Pain in the low lumbar spine, with or without radiation to the hip and leg, is most frequently caused by a pathological condition in the fourth or fifth intervertebral disk. This lesion is difficult to demonstrate. Many patients present few if any objective signs, and, therefore, the diagnosis may depend on the history. Routine roentgen examination seldom reveals worthwhile information except in a negative way. Such films will eliminate fractures of the vertebrae, malformations, arthritis, infection such as tuberculosis, and other causes of backache. Myelographic examination will show a filling defect when the herniation is large enough and situated in such a way to produce a defect. When a large herniation is present, the physical examination will usually suffice to arrive at the correct diagnosis. The primary treatment of lumbar disk herniation should be conservative. Bed rest; traction; rest in flexion; postural exercises; plaster casts; braces, and physical therapy, such as motorized intermittent traction, achieve satisfactory results in a large percentage of cases. Conservative treatment must be continued for a long period after the symptoms have subsided. Surgery should be done only after conservative therapy has failed.

COMPLICATIONS

The complications in patients without neurological signs may be avoided if the definitive treatment is delayed for a few days. Many surgeons believe there is no reason to delay reduction and proceed to reduce and apply a plaster jacket within the first two days. In the young person this may be advisable. In the older patient I usually delay the application of the cast because of the abdominal distention that occurs on the third or fourth day. This complication may be avoided by the use of a mild laxative and mineral oil. Enemas should be used to keep the intestinal contents moving. On the fifth or sixth day the condition of the patient is so improved that reduction and application of the hyperextension plaster jacket may be done. Activity is encouraged immediately. In the old and debilitated patient I consider the compression fracture of the spine to be secondary to the general welfare of the patient. If there are no contraindications, the patient is allowed to be up for short periods of time for bathroom privileges. Plaster casts are seldom used in such cases. A well-fitted corset, reenforced with steel stays, is applied. Urinary retention is infrequently encountered in the patient with uncomplicated fracture of the vertebrae. If it does occur, the care is that given to the patient with neurological complication.

Paraplegic Patient.—Of all the complications besetting the paraplegic patient, those concerned with the emptying of the bladder and maintaining infection of the urinary tract at a minimum offer the greatest challenge. The care of the urinary tract properly belongs to the urologist. The plan of management must be instituted early. Fluids must be given freely, with 3,000 cc. the minimum intake in 24 hours. The Foley type of indwelling, self-retaining catheter is preferred. The management of the catheter requires rigid aseptic technique. The insertion of the catheter should be done expertly, because injury to the in-

sensible urethra must be avoided. The 16 or 18 F. catheter should be changed about once weekly. Thorough cleansing irrigation must be done twice daily and always with the most meticulous aseptic precautions to prevent infection. Antibiotics should be used only when there are indications for such. Ammonium chloride to acidify the urine may be used periodically. When the catheter is changed, a period of trial without the catheter will give information regarding the return of bladder reflex. Recording of the residual urine after voiding will be a guide in lengthening the periods without the catheter and an index of ability to empty the bladder. The patient with complete paraplegia will require the indwelling catheter much longer than one with an incomplete lesion. Complications attributed to the catheter, such as urethritis, epididymitis, periurethral abscess, and calculus, can be minimized by adherence to a rigid aseptic management and well-controlled fluid intake. Mobilization of the patient as early as possible is of the greatest importance in avoiding calculus.

The intestine, like the bladder, is atonic in the paraplegic patient. Adequate care will lessen the number of involuntary stools and facilitate the maintenance of the cleanliness that is so necessary for the care of the skin and prevention of decubitus ulcers. Regularity in emptying the intestine has great influence on the return of tone and reflex in the lower part of the intestine. Mineral oil and laxatives prevent impaction in the rectum. Enemas at regular intervals or manual emptying of the rectum should be used as indicated. Decubitus ulcers are difficult to heal, and, therefore, prevention is highly desirable. Inspection every time the patient is turned will reveal signs of impending danger. The elbows, scapulas, sacral area, anterior superior iliac spines, greater trochanter, ankle malleoli, and heels are the sites frequently involved. The bed must be clean at all times. A wet bed for one hour may start the skin to break down. A wrinkle in the bedding may interfere with the circulation of the skin of the debilitated patient and cause irreversible damage. The skin must be cleansed with soap and water followed by thorough dusting with powder each time the patient is turned. A high protein diet is advisable to maintain the general condition of the tissues. Frequent blood transfusions, during the period of negative nitrogen balance, are of great value.

Mobilization of the patient should begin early and be increased as the condition of the patient will allow. Frequent turning of the patient is the first effort to mobilization. A trapeze hanging from the head of the bed will encourage the patient to use it and thereby maintain strength in the arms, shoulder, and chest musculature. The back rest should be raised as early as possible to facilitate urinary drainage, stimulate the circulation, and keep the patient interested in his surroundings. Almost every patient regards the first use of the back rest as a sign of progress. Mobilization of the patient is of the utmost importance in the prevention of complications, especially those of the urinary tract. Activation of the patient progresses gradually to rehabilitation. The patient with an injured spine, especially the patient with paraplegia, must be treated and observed as a whole and followed and guided until physically and psychologically rehabilitated.

25 E. Ohio St.

DRUGS USED IN TREATMENT OF PATIENTS WITH PETIT MAL EPILEPSY

A SERIAL EVALUATION OF NEW AND STANDARD DRUGS WITH ALTERNATE PLACEBO BASELINES IN IDENTICAL CASES

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In a search for new drugs for patients with petit mal during the past several years, it became apparent to us that contradictory reports by various investigators were largely the result of lack of uniformity in presenting data and of differences in the nature of the case load itself. We felt that since the first aspect of the problem was largely statistical, this could greatly be improved by reporting results systematically and in some detail. The second difficulty—until there is more unanimity of opinion on diagnostic category—can, we believe, be minimized by the use of identical cases for all drugs evaluated. It was also clear that the effectiveness of new compounds could not be judged by comparison with each other or with standard drugs unless a standardized method of evaluation was used for all drugs tested. Since a solution to this problem is important, both to the epileptologist and the general medical public, this paper represents an attempt to evaluate five anticonvulsant drugs by a standardized method of evaluation.

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MATERIALS AND METHODS

In order to compare the relative effectiveness of two standard and three experimental drugs, 72 clinic patients were studied for a period of two years. All of the patients were given the same medication for the control of petit mal seizures, and placebos were alternated with drugs to minimize possible carry-over effects of drugs. We divided the group into two parts to avoid errors in interpretation that might be due to positional effect of a drug.

One-half of the patients, or 36 identical cases, were given placebos and drugs in forward order (group 1), and one half, or 36 identical cases, were given placebos and drugs in reverse order (group 2). Table 1 shows the

order in which medication for patients with petit mal was given, each drug and placebo being given for eight consecutive weeks. Phenobarbital and trimethadione (Tridione) were selected to be the standard drugs tested in this experiment because they have become generally accepted drugs by the medical public for the treatment of patients with petit mal epilepsy. Phenobarbital has been used consistently and persistently for many years, and trimethadione, while used more recently, has been considered an alternate drug, equal or superior to phenobarbital in its anticonvulsant action.

As one of us (F. T. Z.) reported previously[1] of all the newly synthesized compounds for the treatment of patients with petit mal seizures that we have tested, that group of compounds known chemically as the succinimides has proved most promising to date. From this group, we selected for the present experimental evaluation, the three drugs that seemed superior to all others, both in anticonvulsant action and relative mildness of toxic side-reactions. As may be seen from table 1, the three succinimide compounds that we evaluated in this series are Milontin (N-methyl-α-phenylsuccinimide), PM 396 (N-methyl-α,α-methylphenylsuccinimide), and PM 449 (α-ethyl-α-phenylsuccinimide). For the sake of brevity, hereinafter these three compounds will be referred to by their laboratory numbers. All drugs and placebos were made up in 0.3 gm. capsules identical in size, color, and shape, regardless of the drug content, so as to eliminate cues for the patient. Patients were unaware that placebos were introduced, and all drugs and placebos were numbered so that the identity of the medicament was completely disguised at all times. When unwarranted psychological fixation on a particular drug occasionally occurred, the drug number given to the patient remained the same and a private symbol was used to direct the investigator to change the drug, without the patient's knowledge.

Classification of Attacks.—We used an empirical basis of classifying petit mal seizures in this experiment, i. e., one that is based on direct clinical observation of seizures. We consider this preferable to diagnosis made solely on electroencephalographic recording, not only because an electroencephalographic machine is available only to large hospitals and thus limited in its use but because confirmation of the presence of petit mal seizures is not always possible in electroencephalographic recordings. In this present experiment, however, we did have electroencephalographic recordings made of most of the patients, and the classical spike and wave pattern typical of petit mal is clear in all instances. By the use of the empirical method it was also possible to make the drug conform to the clinical definition in judging its effectiveness on the petit mal type of seizure.

While all patients in this series had petit mal, other types of seizures were also present often in the same patient, so the cases were divided into the following categories according to type of clinical attack: (1) pure petit mal (pyknolepsy) form of epilepsy that manifests itself in transient loss of consciousness only, with no concomitant motor phenomena (19 cases [26%]); (2) mixed petit mal form of epilepsy that manifests itself predominantly in transient loss of consciousness and minor motor phenomena (eight cases [11%]); and (3) petit mal combined with other types of seizures such as grand mal (41 cases, or 57%) or psychomotor epilepsy (4 cases, or 6%).

Only one drug was given to any patient at one time for control of the petit mal type of seizure. When petit mal existed along with grand mal or psychomotor epilepsy, however, it was necessary, especially in the case of grand mal, to give diphenylhydantoin (Dilantin) sodium or Mesantoin (ethyl-3-methyl-5-phenylhydantoin) along with the petit mal medication for the control of the grand mal type of attack. Results reported in this experiment are concerned with only the petit mal component and the effectiveness of the various drugs that were given.

Method of Recording Attacks.—Each patient in this experiment kept daily calendar sheets on which he recorded the number of attacks that occurred. These sheets were brought to the clinic each time the patient was given medication, and a duplicate was made of the record sheet for further statistical analysis and for permanent record. In this way, attempts were made to minimize errors in memory often found when patients report retroactively on visits to the clinic.

Results.—Results of this experiment are based on 72 patients who received the entire series of placebos and drugs over a two year period of study. Thirty-six of these patients were given placebos and drugs in forward order (group 1) and 36 in reverse order (group 2). Identical cases thus are used in estimating the effectiveness of the medicaments administered. Originally we started with a much larger number of patients (100), but the size of the group was reduced to 72 at the end of the experimental period for three reasons. 1. Eleven patients were unreliable and failed to return regularly to the clinic or left permanently. 2. Thirteen patients were completely controlled on an experimental drug followed by a placebo, i. e., for eight or more weeks before the last drug in the series was given, and had to be eliminated. For example, if a patient was completely controlled for four consecutive weeks on Milontin and following this remained controlled for four more weeks on a placebo, he was dropped from the series and was not given phenobarbital, trimethadione, PM 396, or PM 449. This is because we felt that a zero baseline would be of little value in judging the effectiveness of subsequent drugs. We are aware that the procedure of eliminating completely controlled cases in this manner not only reduced the number of patients available for experimentation, but heavily weighted our data with intractable cases. Results that are given in the following tables are based entirely on cases in which complete control was not obtained on a drug followed by a placebo for at least eight weeks. 3. Four more patients finished group 1 than group 2, so four patients with a very low incidence of weekly seizures originally were eliminated to equate the size of the groups.

A variety of methods was used in evaluating results from drugs and placebos given in this experiment, and one criterion of judging the effectiveness of any particular medicament was to note the number of average

1. (*a*) Zimmerman, F. T.: Use of Methylphenylsuccinimide in Treatment of Petit Mal Epilepsy, A. M. A. Arch. Neurol. & Psychiat. **66**: 156 (Aug.) 1951. (*b*) Zimmerman, F. T.: New Drugs in the Treatment of Petit Mal Epilepsy, Am. J. Psychiat. **109**: 767 (April) 1953.

weekly seizures that occurred and the percentage of reduction in seizures for each drug or placebo in serial order, using the drug or placebo immediately preceding a particular drug or placebo as a baseline in estimating effectiveness. Table 1 gives the results for those patients given drugs and placebos in forward order (group 1) and those given placebos and drugs in reverse order (group 2), when average weekly seizure rate is used as a criterion of progress.

Table 1 shows that in group 1 there was an average weekly seizure rate of 96 at the beginning of treatment and that at the end of the experimental period this had been reduced to 52 per week, (or 54% of the original rate). For group 2 the average weekly seizure rate at the beginning of treatment was 109 per week, which was reduced at the end of the experiment to 59 per week, (or to 55% of the original rate). Table 1 also shows that with the exception of phenobarbital, positive results, i. e., reduction in seizures, occurred whenever experimental drugs were given and when trimethadione was administered (standard drug), and negative results obtained, i. e., increase in seizures, whenever placebos were administered. It is also apparent that the over-all reduction in seizures is practically identical for group 1 and group 2, suggesting that the order of drugs was of no importance if the over-all rate of seizure reduction at the end of the entire period is considered as the sole criterion of success. This table further shows that trimethadione was most dramatic in reducing seizures under the conditions of this experiment if reduction in seizure rate is used as a criterion of success. For group 1 and group 2 it is plain that regardless of the order in which drugs and placebos were presented, the order of effectiveness in reducing the average weekly rate of seizures was as follows: (1) trimethadione, (2) PM 396, (3) PM 449 (group 1) and Milontin (group 2), (4) phenobarbital (no effect), and (5) placebo (no effect).

TABLE 1.—*Order of Medication, Average Weekly Seizure Rate, and Percentage of Reduction in Seizures*

Drug No.		Av. No. Seizures	Reduction in Seizures, %
Group 1 (36 Patients)			
1.	Placebo	96	..
2.	Milontin *	98	3
3.	Placebo	98	— 5
4.	Phenobarbital	103	— 5
5.	Placebo	116	—12
6.	Trimethadione (Tridione)	49	57
7.	Placebo	51	— 4
8.	PM 396 †	45	12
9.	Placebo	56	—24
10.	PM 449 ‡	52	7
Group 2 (36 Patients)			
9.	Placebo	109	..
10.	PM 449 ‡	101	7
7.	Placebo	103	— 2
8.	PM 396 †	64	38
5.	Placebo	68	— 6
6.	Trimethadione	41	39
3.	Placebo	49	—19
4.	Phenobarbital	56	—14
1.	Placebo	63	—12
2.	Milontin *	59	6

* N-methyl-α-phenylsuccinimide.
† N-methyl-α,α-methylphenylsuccinimide.
‡ α-ethyl-α-phenylsuccinimide.

The data were also grouped into the categories of complete control, (100%), i. e., absence of seizures for a period of at least four consecutive weeks, practical control (80 to 99%) reduction in seizures, partial control (5 to 79%) reduction in seizures, and no effect (4% or less) reduction in seizures. The classification of "worse" was also included when seizures increased. We used these categories for judging the effectiveness of medication because of their usefulness clinically in evaluating results. Data obtained from each of the five placebos and five drugs given were subjected to analysis under this criterion, and all possible combinations of drugs and placebos were used for comparison. For example, each drug and placebo was compared with the drug or placebo immediately preceding it, and the last drug was compared with all the others in the forward order of medication, while the next to last was compared with all others in the reverse order of medication. Statistical analysis of all of these various combinations is complicated, and, for the sake of clarity, we have limited results reported here to a comparison of the two standard and three experimental drugs given, i. e., phenobarbital, trimethadione, Milontin, PM 396, and PM 449, keeping in mind that a placebo intervened between each drug.

TABLE 2.—*Percentage of Control Obtained in Group 1 with Each Drug, Using the Drug Immediately Preceding as a Baseline for Judging Results*

	Phenobarbital Over Milontin	Trimethadione Over Phenobarbital	PM 396 Over Trimethadione	PM 449 Over PM 396
Complete control	0	0	17	3
Practical control (80-99%)	3	17	8	0
Partial control (5-79%)	50	38	36	11
No effect (0-4%)	5	14	19.5	8
Worse	42	31	19.5	78

Table 2 shows the degree of seizure control obtained for each drug in the forward series (group 1) when each drug is compared with the preceding drug. It may be seen from table 2 that for the first group of patients studied PM 396 showed the highest degree of complete control obtained, trimethadione the highest degree of practical control, and phenobarbital the highest per cent of partial control. When the categories of practical control (80-99% seizure reduction) and complete control (100% seizure reduction) are grouped together, however, in order to judge the effectiveness, i. e., when a very high standard of degree of control is used as a criterion, the following findings are clear: Phenobarbital gives only a 3% improvement over Milontin, trimethadione gives a 17% reduction over phenobarbital, PM 396 gives a 25% reduction over trimethadione, and PM 449 gives only a 3% reduction over PM 396.

Table 3 gives the degree of control for each drug in reverse order (group 2). Results of table 3 show that for the second group of patients PM 396 again showed the highest percentage of complete control as it did in group 1. PM 396 and trimethadione gave equal practical control and phenobarbital the highest percentage of partial control when each of these drugs is compared with the drug

immediately preceding it. When the categories of complete control and practical control are grouped together, the following findings are shown: PM 396 gives a 30% reduction over PM 449, trimethadione gives a 17% improvement over PM 396, phenobarbital gives no reduction over trimethadione, and Milontin gives a 16% further reduction over phenobarbital. From both of the groups, using the criterion of complete control plus practical control, the data suggest that regardless of the order of the drugs PM 396 and trimethadione are far superior to the other drugs tested in this way.

We also treated the data by another method in order to analyze results, since we were interested in learning how the patients progressed for the entire period of the experiment. We therefore used the original placebo baseline as a criterion for evaluating all of the drugs used and compared the effectiveness of each drug with results obtained while the patients were on the first placebo of the series. Results of this phase are given in table 4 for group 1 and in table 5 for group 2. In this series of drugs, using

TABLE 3.—*Percentage of Control Obtained in Group 2 with Each Drug, Using the Drug Immediately Preceding as a Baseline for Judging Results*

	PM 396 Over PM 449	Trimethadione Over PM 396	Phenobarbital Over Trimethadione	Milontin Over Phenobarbital
Complete control	15	2	0	5
Practical control (80-99%)	15	15	0	11
Partial control (5-79%)	55	56	74	44
No effect (0-4%)	0	17	14	20
Worse	15	10	12	14

the first placebo as a baseline, it may be seen from table 4 that PM 396 gave the highest percentage of complete control and trimethadione the highest percentage of practical control. Trimethadione showed the highest number of cases in the partial control classification. If the categories of complete control and practical control are again combined in interpreting all of the data, the order of effectiveness is much the same as previously described when the drug immediately preceding any given drug was used as a baseline. PM 396, trimethadione, PM 449, Milontin, and phenobarbital gave complete plus practical control in the following percentages: 38, 25, 17, 13, and 11 respectively. A comparison of the placebo (no. 1) and PM 449, which was the last drug given in the forward series,

TABLE 4.—*Percentage of Patients Controlled in Group 1 with Each Drug, Using the First Placebo (No. 1) as a Baseline for Judging Results*

	Milontin	Phenobarbital	Trimethadione	PM 396	PM 449
Complete control	8	0	0	19	3
Practical control (80-99%)	5	11	25	19	14
Partial control (5-79%)	40	44	55	31	38
No effect (0-4%)	18	14	3	8	14
Worse	29	31	17	22	31

shows the over-all gain in terms of the patient's total progress for the two year period study and how much seizures had been reduced on an average. If this is done, it is clear that 3% of the patients were completely controlled at the end of the experiment (in addition to 13 patients eliminated from the experiment because they had been completely controlled during the series on a drug followed by a placebo).

When drugs were given to group 2 in reverse order and a comparison of the series with the first placebo given is made, the results obtained are given in table 5, which shows that PM 396 gave the highest percentage of complete control and trimethadione the highest percentage of

TABLE 5.—*Percentage of Patients Controlled in Group 2 with Each Drug, Using the First Placebo (No. 9) as a Baseline for Judging Results*

	PM 449	PM 396	Trimethadione	Phenobarbital	Milontin
Complete control	9	22	0	0	10
Practical control (80-99%)	0	9	20	0	10
Partial control (5-79%)	48	28	53	49	50
No effect (0-4%)	24	25	13	30	10
Worse	19	16	14	21	20

practical control, as in the forward series. Trimethadione also gave the highest percentage of partial control, although phenobarbital and Milontin were practically identical, showing 49% and 50% partial control as against the 53% partial control obtained with trimethadione. When the categories of complete control and practical control are combined for group 2, the order of success is quite similar to that secured in group 1 when an initial placebo baseline is used for estimating the effect of subsequent drugs. PM 396, trimethadione, Milontin, PM 449, and phenobarbital gave complete plus practical control in the following percentages: 31, 20, 20, 9, and 0 respectively.

We believe these results for all patients, regardless of the order in which the drugs are used, definitely show that when a high standard of seizure reduction is required, all of the experimental drugs (PM 396, PM 449, and Milontin), as well as trimethadione, are definitely effective to a higher degree than is phenobarbital in ability to control petit mal seizures. We also feel that this high degree of

TABLE 6.—*Percentage of Seizure Control, Using an Initial Placebo Baseline*

	Average of All Cases	Group 1	Group 2
Trimethadione	76.5	80	73
PM 396	64	69	59
Milontin	61	53	70
PM 449	56	55	57
Phenobarbital	52	55	49

seizure control, i. e., one in which seizures are reduced at least 80%, is a good method for evaluating results and comparing the effectiveness of different chemical compounds.

Finally, for the sake of completeness, the categories of complete control, practical control, and partial control were combined, and results were considered from this viewpoint. When some degree of seizure control, i. e., from 5 to 100%, is used to compare the effect of medication on identical cases, and an initial placebo baseline is used, it was found that all of the drugs used showed good anticonvulsant action. Results of this aspect of the study are given in table 6, which indicates that all of the drugs showed good anticonvulsant action when the criterion of some degree of seizure control was used, reducing seizures from 52 to 76.5% when data from the two groups are averaged and from 49 to 80% when they are treated separately. It is likewise apparent that when this wide

range of seizure control is allowed and credit given for reduction in seizures as low as 5% of the original rate, phenobarbital makes a much better showing than it does when a high degree of seizure control is demanded. We believe that these data indicate that contradictory results reported by investigators are dependent to a large extent on confusion in definition as to the degree of control credited to drugs, and that too wide a range of control, as in table 6, reduces the differential value of drugs for patients with petit mal. In our opinion the category of practical control becomes the critical one both statistically and clinically for comparing the effectiveness of medication, since we find that it is rare for patients to remain in the category of complete control for long periods of time and that cases lost eventually fall into the classification of practical control, with an occasional seizure being seen. On the other hand, if too wide a range is allowed, it is very difficult to get an accurate basis for the comparison of drugs.

We also believe these data reveal that in spite of the introduction of placebos, there is a definite carry-over effect to the next placebo or drug after treatment with an effective type of medication. Lennox [2] mentioned this in the use of trimethadione and stated that when no medication followed trimethadione in his patients, trimethadione was credited with holding for "weeks or months." The longest period that Lennox reports is 18 months for the carry-over effect of trimethadione. Results of the present study confirm Lennox's work so far as trimethadione is concerned and, we feel, present evidence that whenever effective medication is given seizures tend to show a downward trend on subsequent medication, or one which is much nearer to the average reached by the effective drug than to a previous baseline. The tentative conclusion that we draw from our data on this problem is that a constant revision of the baseline is necessary over a period of years to judge the relative effectiveness of drugs because of this possible carry-over effect. There is also the additional factor of length of treatment to be considered in judging results, since we have noticed that the majority of patients seems to improve over a period of years regardless of what medication has been given.

DOSAGE

In this experiment a standard dosage of one capsule per day for the first week was given. As we mentioned previously, the capsule was 0.3 gm. in size, regardless of the content. Unless a toxic condition appeared, the dose was increased by one capsule each week for the next three weeks, until a maximum of four capsules per day was given to all of our patients. For trimethadione (0.3 gm.), phenobarbital (0.015 gm.), PM 396 (0.3 gm.), and PM 449 (0.1 gm.), the range of dosage from three to four capsules per day was adequate for estimating the effective control of petit mal. In the case of Milontin (0.3 gm.), one of us (F. T. Z.) reported previously [1a] that an average dose of 2.4 to 2.7 gm. per day, or from eight to nine capsules per day was the most effective dose for most persons. In the present experiment, however, this level could not be reached in an interval of eight weeks, without pushing the dose up very rapidly. The latter would, of course, not only have sacrificed scientific accuracy by a change in the standard procedure but might have adversely affected the welfare of the patient. We therefore considered it preferable to sacrifice optimal results on Milontin because the dosage was concededly too low than run the risk of introducing toxic effects because high doses were reached too quickly. We believe that we did not reach the degree of success with Milontin in this experiment such as one of us (F. T. Z.) reported formerly [1a] because of this low dosage factor.

TOXIC SIGNS

Throughout this experiment no serious toxic signs appeared from any of the drugs given, and there were no serious blood dyscrasias, such as are sometimes reported with trimethadione. All blood and urine studies were within normal limits. In our experience, most of the toxic signs that we reported appeared at very high dosage levels, except for occasional individual idiosyncracy to a drug, and in the present experiment high dosage levels, especially on the experimental drugs, PM 396, PM 449, and Milontin, were automatically avoided by the conditions under which medication was administered.

SUMMARY

In an attempt to secure a serial evaluation of drugs for identical patients with petit mal, we introduced a variety of drugs and placebo baselines as criteria of effectiveness and rotated the order of the drugs systematically. Results indicate that all of the drugs given have good anticonvulsant action if a wide range in degree of seizure control (5 to 100%) is used to evaluate findings. If a high standard of seizure reduction is introduced as a criterion of success, such as practical control (a minimum of 80 to 99%), then PM 396 and trimethadione are definitely the drugs of choice. Over the long treatment period of two years, no difference in the rate of average weekly seizures was apparent whether drugs were given in forward or reverse order, and in both of our groups seizures per week were reduced almost 50% at the end of the experiment. The order of drugs did seem important, however, during shorter intervals of time. Our findings suggest that subsequent medicaments tend to show the same or a higher level of seizure control after an effective drug, and the carry-over effect of trimethadione reported by Lennox [2] is confirmed by our present data.

By using a standard dose in all cases, we introduced an adequate dosage level for trimethadione, phenobarbital, PM 396, and PM 449, but penalized results with Milontin, in which a higher average dose is required optimally. No serious toxic signs appeared from any of the drugs given, and hematological and urinary findings remained within normal limits. In treating our data statistically and breaking down results into categories for judging degree of control, attempts were made to show the advantage of specificity in definition for judging the effectiveness of medication in reporting results generally. Our findings also point to the need for a periodic revision of a baseline over a long interval of time, so that greater accuracy may be obtained regarding the relative value of medication for patients with petit mal, regardless of the type given.

11 E. 68th St. (21) (Dr. Zimmerman).

2. Lennox, W. G.: Tridione in the Treatment of Epilepsy, J. A. M. A. **184**: 138 (May 10) 1947.

THE LITTLE STROKES

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One of the commonest diseases of man is that in which, over the course of 10 or 20 years, a person is gradually pulled down by dozens or scores of thromboses of little arteries in the brain. Dr. James Kernohan,[1] pathologist of the Mayo Clinic, said, on examining tissues from brains, these are among the commonest of the lesions he finds. Today most physicians know the syndrome of "the little strokes," but, I am sorry to say, the diagnosis is still often delayed and usually for two reasons 1. The patient often fails to tell the physician of a bad dizzy spell at the start of his trouble. 2. The physician is not well enough acquainted with the more bizarre and puzzling of the symptoms that can result from little strokes. Obviously, the syndrome must vary greatly with each patient, depending largely on the position in the brain of the tissue destroyed. In most cases there are no weakened muscles, no trouble with speech, and no areas of anesthesia, because the thrombosed arteriole was in a "silent area." In such cases the patient may suffer only from changes in character, in ability, in judgment, or in emotional stability, changes that he does not think to mention. Probably, in most cases, he does not realize how much he has failed. Usually, these changes can be learned about only if the physician questions the relatives whose statements may show in a few minutes that the man's brain has been severely injured.

Recently I saw a 65-year-old physician who, some weeks before, had been incapacitated by a pain in the abdomen, which his friends had thought must be due to an ulcer; however, studies in several clinics showed nothing. Sensing that the man was slowing down both mentally and physically, I spoke to his wife who said that the trouble had begun one day when, for 20 minutes, her husband had been confused and unable to talk. Since then he, who had always been so kind and good, had been unreasonable and irascible. One day he had even turned on his adored granddaughter and had cursed her violently. As the wife said, he was so changed she hardly knew him. Because, in the eight years that have elapsed since I wrote my main article on this subject,[2] I have seen hundreds of such cases and have learned of new symptoms of the disease, I have decided to give here a brief summary of the syndromes as I know them or suspect them today. I say "suspect" because it is often impossible to be certain that a particular short spell of giddiness or mental confusion was due to a stroke. One cannot be certain of the cause of some trying paresthesia in the case of an elderly person, but a physician becomes more and more certain of the nature of a certain syndrome after he has seen it appear many times in the cases of older persons who seemed to be dying slowly from the effects of arteriosclerosis of the brain.

LITTLE STROKES ARE EPISODES IN A LONG ILLNESS

I have found a few descriptions of individual cerebral thromboses in recent literature, but rarely a description of the disease as a whole; the disease that commonly takes years to kill the patient. It is this long-lasting and slowly killing disease that physicians must recognize early in its development. Often, when a suspicious episode is seen, if only the physician would ask the relatives to remember some peculiar spell followed by changes in character and ability, they will tell him that the disease must have started many years before. I doubt if I would ever have learned to recognize the long-lasting syndrome of the little strokes if I had not had the opportunity to watch the unfolding of the whole disease in the cases of a few relatives and old friends. So far as I can learn, the disease in its entirety remained practically undescribed until recent years when my first papers on it appeared. The reason why descriptions of the whole syndrome were slow in coming was that consulting physicians so rarely see more than some one episode of the disease. For instance, the hotel physician who, one morning in 1913, called me, as a gastroenterologist, to see an elderly woman who had waked vomiting, assumed that what she had was an attack of "acute indigestion." He thought it was all due to some oysters eaten the night before. The minute I examined her I noted a slight weakness of the woman's right arm and leg. When I called her daughter's attention to this, she said, that early that morning the weakness had been much worse and the mother had had to lean heavily on her to get to the bathroom. The story of many previous attacks indicated slight sudden injuries to the brain. As the years passed, I watched the woman die slowly with thromboses of small arteries in several parts of the body. I knew then that, on that morning in the hotel, what I had seen had been just one episode in a fatal disease that had been producing symptoms for at least eight years and that was to go on producing them until the patient died.

In the case of one of my relatives, little strokes began to hit his brain in 1890, before he was 40. During the next 15 years I watched him die slowly with one puzzling episode after another. One was thought to be an attack of influenza, others were called nephritis, walking typhoid, and a heart attack. Eventually, one morning, he awoke with a temporary weakness of one leg, and then, at last, my professors and I were sure of what he had. Today I know that all of those spells were probably episodes in the course of one disease—intracranial arteriosclerosis. In the man's early 50's he died with a big stroke. Later, I watched his wife's brain being destroyed in the same way over the course of 10 years. A friend of mine, the head of a big business, was afflicted for 23 years before he died. The first episode, when he was about 45, was a definite stroke with weakness and clumsiness of the right hand. He recovered from this so quickly that none of the physicians, including myself, could believe that he had had a stroke. We thought it a harmless spasm, and, because we did not understand the story, we largely ignored it. With the second one, he apparently fell into some moving machinery, and the hand which he put out to save himself was mangled. With the third little stroke, which came silently in the night, so much of his brain was injured that he never again could work. During the next 20 years before death the patient had paralysis agitans (Parkin-

1. Kernohan, J.: Personal communication to the author.

2. Alvarez, W. C.: Cerebral Arteriosclerosis with Small, Commonly Unrecognized Apoplexies, Geriatrics **1**: 189 (May-June) 1946.

son's disease) and finally a general paralysis. As Osler said, many of us take as long to die as we do to grow up. Speaking of Oliver W. Holmes, Osler said Holmes went quickly. "His friends were spared the most distressing of all human spectacles, those cold gradations of decay, in which a man takes nearly as long to die as he does to grow up, and lives a sort of death in life, 'ita sine vita vivere, ita sine morte mori'." [3] I remember a man who lived for 30 years after he had been made childish by a series of three little strokes that did not affect either his speech or his muscles.

SYMPTOMS

A little stroke may be suspected whenever (1) a man or woman past 38 or so has a mental and nervous disability that is out of all proportion to the little indigestion, abdominal, or thoracic pain complained of, (2) a nervous breakdown or a queer group of symptoms come suddenly on a certain day, and (3) one learns from the family that, after a dizzy spell, blackout, or perhaps a fall, there came changes in character and perhaps an inability to work.

Mental Changes.—Recently a 50-year-old executive was referred to me for treatment of a supposed duodenal ulcer, diagnosed because a few indefinite changes appeared in the roentgenograms. Because the man's complaint was not that of hunger pain but rather of feelings of weakness, "queerness in the head," depression, and inability to work comfortably, I questioned his wife and learned that the illness had appeared after two brief spells when he had become mentally confused and had fallen down for a moment. Many of these syndromes are easily recognizable for what they are when the patient and family date them from a sudden "collapse," fall out of a chair, sudden momentary loss of the sense of balance, spell of "acute indigestion" with vomiting, or spell of mental confusion. Often, when one recognizes that a man has had some sudden, small injury to the brain, one cannot get the story of a little stroke because it may have come during the night or it may have come without producing any accompanying disturbance. To show how little shock a thrombosis in the brain may produce, recently I saw a physician who had just had a big stroke with complete paralysis of half his body. He assured me that, as he had fallen, he had felt no shock or pain, and, in fact, no distress at all, except that of realizing the implications of what had happened to him. Such cases have made me see why so many of the little strokes must come without any immediate symptoms. To show what occasionally happens when a fairly large stroke comes during sleep, one morning an able executive who had had a phenomenal memory, woke to find himself with the poor memory of an old man. A few months later he had another little stroke that left a small area of anesthesia around the left corner of the mouth. In many such cases one cannot be sure about an episode until the patient comes back with the history of two or three more spells, one or more of which was definite.

Changes in Character.—Very significant is a history of a change in character. Often the wife, after repeated questioning, will admit that on one or more occasions in the past, she was appalled and puzzled when a previously kind, affectionate, and gentle husband suddenly began to explode in anger over almost nothing. A man who used to be a tower of strength to relatives may have become mentally weak, querulous, and weepy. A formerly much-loved son may be puzzled to find that his father will no longer trust him even to go to the bank to deposit a few dollars for him.

Loss of Ability.—At the patient's office his business associates may become distressed over his loss of ability and drive. No longer can the man get things done, and no longer can he get along comfortably with the people about him. He may have become so irascible and unreasonable that he is of no further use to his company. Often his president will send him for a complete check-up at three or four big clinics and will then be puzzled when the man comes back each time with a report that he is all right because, to all tests, he reacted normally. Many such men lose their old business judgment, do foolish things, and lose money. Some men, after a little stroke, lose their moral sense and get into scrapes with women.

Premature Aging and Slowing-Up.—Often the wife, if asked about sudden aging, will say, "Yes, after that peculiar spell of his, he suddenly changed into an old man, a man so different that now I hardly know him. He is no longer my old lover and chum. He is a querulous, depressed, and irascible man, who sometimes breaks down and cries. He will talk now only about the misery in his head and his bowels. He has lost much of his old refinement, and he now hates to take a bath or to change his clothes. Also, he has lost his sexual potency." An observant physician can often see what is wrong as the fellow walks into the office, perhaps with the hesitant, short, weak steps of an old man. Commonly, I make the diagnosis as the man gets up out of the chair in the waiting room; he is so clumsy about it. I often make the diagnosis in a moment when I see how dull the man looks and how much older he is than his chronologic age. Often he is not well groomed. He will no longer have the alert, attractive appearance of an executive or even a good clerk or salesman. After a few little strokes a banker may look so stupid that one would not think of hiring him as a janitor. Curiously, interns and residents rarely notice these tremendously important physical findings. They look only at the roentgenograms. The patient may be talking out of one corner of his mouth because of a slight weakening of some of the facial muscles; he may be poorly shaven, with much of the formerly alert expression having left his face, he may complain of ear noises and a lack of a good sense of balance; and he is afraid at times that he will fall.

Fear of Being Alone.—Highly significant is the fact that a man, who was once fearless, is often afraid of being left alone in the house. These people fear being suddenly so crippled by another stroke that they will be unable even to reach the phone and call for help. Actually, this does happen sometimes. I remember a fine-looking man of 70 who spent a cold winter night, clad only in pajamas, lying on the bathroom floor. He had to lie there until his daughter came the next morning to see why he had not come down to breakfast. By evening he was well, and he remained well for the next 10 years. Another man, living alone in an apartment, got a little stroke while he was in the bath tub. Unable to get out, he eventually managed to summon the janitor by banging on the water pipes with a soap dish.

3. Osler, W.: Oliver Wendell Holmes, Bull. Johns Hopkins Hosp. 4: 85, 1894.

Loss of Old Interests and Joy in Life.—Often a woman, after a little stroke, will lose most of her old interests in husband, children, and grandchildren. She will let her house go uncared for, will refuse to see old friends, and will begin tucking things away here and there, where later she cannot find them. These patients will often say that in a moment they lost all of their old sense of well being and all of their old zest for life. Some say they "just feel awful" day and night, and I never found a drug that would help them to feel comfortable again.

Blood Pressure May Be Normal.—Many ask if all these persons have hypertension. Some do, but many do not. They do not need a hypertension to explain the trouble because the lesion usually is a thrombosis of a small artery, which is most likely to come when the blood pressure is low. For this reason probably most of the little strokes come at night, when the blood pressure is at its lowest.

Sudden Drops in Blood Pressure and Weight.—Highly diagnostic of a little stroke is a sudden large drop in a previously high blood pressure. Many a time I have seen the pressure drop to normal and stay there for a month or so, or even for the rest of the patient's life. Highly diagnostic, also, is a sudden big drop in weight due, I imagine, to a change in the setting in some little regulatory center, perhaps in the hypothalamus. I remember a physician's mother-in-law who, in a few weeks, lost 90 pounds and after that, for years, did not lose any more. Other changes, perhaps also in the hypothalamus, may in rare cases produce a sudden severe insomnia, a long-continued slight "fever," or sudden spells of crying unaccompanied by any feeling of sadness.

Changes in Writing, Speaking, and Swallowing.—Diagnostic is the admission of a patient that, after a dizzy spell, his handwriting changed so much that his children complained that they no longer could easily read his letters or that the bank asked him to come in and leave a new signature. Often there is a little difficulty in writing the right word, all of a word, or all of the words intended to go in a sentence; some of them may be left out. Occasionally, for a while, there is some thickness of speech or even a transient aphasia, with difficulty in finding words. In many cases injury to the brain stem will produce such difficulty in swallowing that food will often go down the wrong way and cause choking, strangling, and coughing. The saliva may become thick, ropey, and hard to get out of the throat. A little saliva may drool out of one corner of the mouth. For a time the person may be repeatedly biting his tongue, until he learns again to control it properly.

Pain and Arthritis.—After a little stroke there may come a causalgic type of severe and uncontrollable pain in the hand, wrist, or forearm. In rare cases the wrist or hip on the affected side will quickly develop trophic changes or what looks like an acute destructive arthritis. A severe, atypical neuralgia of the face may occur.

Falling Down Steps.—In asking the patient about a fall he had, one must always pay attention to his claim that the trouble was not produced by the blow on his head; he will maintain that he fell downstairs because he blacked out. Too often a physician fails to accept the patient's statement on this essential point, which makes a difference in the diagnosis and in an insurance suit.

So-Called Heart Attacks.—Today, I think most little strokes, if noticed at all, are called "heart attacks" by physicians. Not having been trained to think of disease in the brain, we rarely do. Also, seeing that persons feel disgrace in having a stroke and none in a heart attack, many physicians, when in doubt, make the diagnosis that will not offend the family. In such cases, especially when, with the stroke, pain has shot down into the thorax, most physicians try for weeks to get an electrocardiogram that will show changes. What is highly significant is that in the months and years after the little collapse it will become obvious that the man never had any anginal pain, shortness of breath, or any other sign of heart trouble. He will be able to walk along the street comfortably. His difficulty will be that his brain no longer works well.

Injury to Both Brain and Heart.—Naturally, when in all parts of a man's body there comes a tendency to the thrombosis of little arteries, one must expect him to suffer injuries to both heart and brain. There is also the possibility that during a severe attack of coronary thrombosis, when for a while the circulation of the brain is poor, some anemic injuries may be wrought here and there in some of the nerve centers. As Dr. Myron Prinzmetal [4] has reminded me that, just as in some cases there are a number of little vascular injuries in the brain, so in many hearts that come to autopsy the pathologist finds many a little white scar due to a silent thrombosis.

Pain That Shoots into the Abdomen.—In those many cases in which, with a little stroke, pain shoots down into the abdomen the patient is lucky if he is not operated on for a supposed cancer. A few times a year I prevent an unnecessary abdominal exploration by (1) drawing out the story of a little stroke, and (2) satisfying the home physician that the little changes in some of the roentgenograms of the stomach do not indicate a cancer. Physicians who themselves once experienced abdominal distress associated with a little stroke have told me that, at the time, they felt as if some organ in the abdomen were being torn in two. One such physician had his abdomen explored twice by surgeons who sought in vain for a cause of his pain and indigestion. In the course of two months the distress faded out. I am sure the surgeons would never have operated if their assistants had only taken a better history and had learned how suddenly the spell had come and how severely it had hit the patient's brain. One of these patients, a physician with abdominal pain after two little strokes, was so weakened by the injury to his brain that for six weeks he was not strong enough either to sit up or to hold his head up. This should have shown everyone that the primary trouble was not in the abdomen.

"Acute Indigestion" and "Ménière's Disease."—The sudden, brief attacks of nausea and vomiting so commonly seen in cases of older persons hit by a little stroke are often supposed to be due to "acute indigestion." Quite a few elderly persons, after a little stroke, suffer from sudden attacks of diarrhea and rarely from rectal incontinence. Many elderly persons who, for a time, complain

4. Prinzmetal, M.: Personal communication to the author.

of chronic nausea, have had a little stroke. Most of the old persons who are thought to have Ménière's disease, with "dizziness," really have no true vertigo, no trouble with their ears, and, hence, no true Ménière's disease. The disease is all in their brain, as one can often see by asking about mental deterioration. It is possible that, in some cases of supposed transient Bell's palsy of one-half the face, the difficulty is really due to a little stroke. I suspect this when the trouble clears in a matter of days, when the person's character changes for the worse, or when there are signs of injury to another cranial nerve. For instance, in the case of a man recently seen with supposed Bell's palsy, careful history-taking showed that with the onset of the facial paralysis he had seen double and had been mentally confused. Usually a kindly, pleasant man, he became arrogant and quarrelsome for a time.

Brief Imitations of a Big Stroke.—In rare cases, for a few minutes after a little stroke, the patient will be unable to say a word; then he will be able to talk perfectly again. This transient aphasia may be associated with an equally temporary weakness of an arm or leg. In such cases most physicians will be strongly inclined to diagnose "spasm" of an artery in the brain. This idea, of course, is comforting to the patient, but I doubt if the diagnosis is often correct. As Osler [5] so wisely used to say, it is better to diagnose a thrombosis of a small artery, perhaps with a momentary shock to the brain, because in so many of these cases the patient later shows signs of a permanent injury; his legs may become "rubbery" and may stay that way.

Injuries to the Brain Stem.—A few patients show signs of injury to the medulla oblongata and its nerves. Many persons, for a time, will speak thickly and with a changed voice, some will choke when they try to eat, and a very few will have so much difficulty in swallowing that they may have to be fed through a stomach tube for the rest of their lives.

Burning and Bad Tastes in the Mouth.—Commonly, in older women and occasionally in older men, there comes a miserable burning in the tongue or mouth, perhaps on only one side. There may also be a foul or metallic taste. When the trouble is only on one side the physician can be pretty sure that it is due to injury in a nerve center. I have seen this syndrome occur so often after definite strokes that now, when I see a person with it and cannot get a history of a stroke, I always suspect that one came during the night. In these cases I have never seen any treatment do any good, and the burning sensation may remain for years.

Burning of the Skin and Other Paresthesias,—Rarely, after a little stroke, a man will get a curious paresthesia of the scalp, with perhaps a feeling of extreme heat or cold. Occasionally, the patient will complain of great burning in a large area of skin. For instance, one day eight years ago, a woman suddenly felt peculiar, a bit woozy, and confused. Ever since then she has had a very distressing burning of the skin over her whole back. An important point is that this area of skin does not correspond to the distribution of any nerve tract. Also, no treatment has ever done any good.

5. Osler, W.: Personal communication to the author.

A Mild, Thalamic Type of Distress.—I have seen several cases in which what looked like a mild, thalamic syndrome came suddenly, leaving a constant, long-lasting "misery" all down one side of the body. In most of these cases the patient has been treated for years for a floating kidney or for a supposed stricture of the ureter. In one case of apparent thalamic syndrome, the woman found her distress on the right side when she awoke from an anesthesia, and it never let up a minute afterward. Interesting was the fact that with this the corresponding half of the vagina became so sensitive that intercourse became painful. It is known that sometimes during anesthesia, if insufficient oxygen is supplied, a center in the brain can be injured.

Blindness.—In rare cases, after a little stroke, the patient will suddenly go blind in one or both eyes. I remember a man of 60 who, while crossing the street, was felled to the ground for a moment with a stroke that promptly took away vision in one eye. It may well be that he had a thrombosis of the internal carotid artery because, in the next few days, the clot seemed to spread over, to produce blindness in his other eye. Some older persons complain of little flashes of light that they see in one eye perhaps toward the outer margin of the field. It seems probable that these are due to some little arteriosclerotic injury to part of the visual center of the brain, but ophthalmologists suspect these are due to slight changes in tension in the eye.

Weakness of External Ocular Muscles.—Occasionally, a little stroke will affect one of the external ocular muscles. A patient with a supposed heart attack may state that he saw double for a day or two. The implications of such a fact must be faced. For instance, a man had a series of little strokes for 25 years before he died. He had his first recognizable one about the age of 30. At that time one external ocular muscle was paralyzed. A few years later he apparently had another little stroke (also not recognized at the time) that suddenly took away so much of his intelligence he could no longer work. His wife immediately had to take over the management of the business. For the rest of his days the man could no longer help because he could not be trusted even to make out a sales slip. At 55 he died after another series of little strokes, one of which produced aphasia for a week. Interestingly, for many years this man was treated only for heart disease. At autopsy some vascular changes were found in his heart, but I was told that the pathologist found far more serious arterial disease in the brain.

Little Strokes That Revive an Old Migraine or Produce Unilateral Headache.—Recently, I have come to recognize cases in which, in later life, little strokes either bring back an old migraine that had faded out years before or produce unilateral headaches perhaps even complete with scintillating scotoma. For instance, a woman who had never had migraine had a little stroke in her 50's. Some time later while out driving in her car, she suddenly had another little stroke so bad that if her sister had not been there to grab the wheel there could have been a bad accident. For some time after this she had unilateral headaches with scotoma. Later, another little stroke wiped out the tendency to the headaches. I suspect that this syn-

drome of unilateral headache in old age may have sometimes the same relation to migraine as certain types of convulsive disorder late in life have to hereditary epilepsy.

A Stroke Can Bring a Psychosis.—Every year I see cases in which the patient, often a woman, after a little stroke goes into an agitated depression in which, in an agony of restlessness, she walks the floor most of the day and the night. Unfortunately, this syndrome is so little known to most physicians that practically all of these patients whom I have seen have been operated on once or twice for gallstones or some other trouble, which had nothing to do with the syndrome. After a patient reaches the age of 50 or 60, little strokes can easily bring out into full development a psychosis. The tendency to psychosis, perhaps for a lifetime, may have been held in check with the help of the person's good sense and great efforts at self-control. Then comes the little stroke, and the patient loses control. Thus, I have seen persons who, after a lifetime of suspiciousness, suddenly, after a little stroke, become dangerously paranoiac.

"Epilepsy" Late in Life.—Some persons who begin to have occasional convulsions late in life may well have had one or more little strokes, perhaps on top of a life-long carrier state of epilepsy.

Brain Tumor.—I have seen several elderly persons with what looked like a little stroke who were almost operated on for a supposed brain tumor. The fact that they later recovered without an operation suggested that the symptoms had been due purely to a stroke.

Little Strokes Early in Life.—Occasionally, I see a person who, in his or her 30's, had a spell typical of a little stroke. It may have left some physical weakness and mental disability. Such a story told by a person of 60 would not puzzle me for a minute, but, in the case of a woman of 30, it is hard to believe she had a stroke. And yet, she could easily have had one. Even soldiers in their 20's have strokes. Oftentimes in the cases of younger persons I have not had the courage to make the diagnosis of a little stroke until later when the patient returned with a history of having had a series of them, one or two of which were definite. In the cases of some few young persons one can recognize the characteristic story of a rupture of a tiny aneurysm on the circle of Willis.

Diagnosis Is Not Always Easy.—Persons with little strokes can easily deceive the physician by not telling all of the essential story. A while ago a woman of 60 went to a university hospital, where she was seen by able internists. She complained of a burning "misery" over her left hip that had been present day and night for four years. This constancy alone should have made the physicians think of an injury to the brain because constant burning or widespread misery almost always has its origin in the central nervous system. Evidently the assistant who took the history failed to learn that the woman had had four typical little strokes, two of them associated with mental confusion, a loss in the sense of balance, and difficulty in writing. One stroke came while she was crossing a street, and she became so confused that men had to run out from the sidewalk to pull her in out of the stream of traffic. Unfortunately, she had forgotten much of this, but her son told me about the several spells, which, in his opinion, had been strokes. When the roentgenologic studies revealed some gallstones, these were accepted as the cause of the patient's distress, and she was turned over for operation. Since her gallstones were silent, produced no symptoms, and could hardly have caused the misery over the left hip, she was no better for the operation. Today, years later, the old distresses still persist unchanged.

WHAT CAN BE DONE?

First, can the disease be prevented? Possibly its onset can be delayed by holding down a person's weight and reducing the amount of cholesterol in the diet. For instance, two stout persons who each died of a long series of little strokes had four children. With such strong evidence of atherosclerosis on both sides of the family, I had feared that two or three of the children might have the disease, but actually, today, all four are in good health in their 60's, perhaps because they all ate sparingly and avoided the stoutness of their parents. People can get better after a little stroke. Many lose the symptoms so quickly that the impression gained is that there was only a little spasm in an artery. In many other cases, after weeks or months, the patient is well enough to go back to work. Sometimes I would not have believed such improvement possible if I had not seen it myself. Things that could have happened were: (1) that the nerve cells were only slightly injured, so that function was quickly recovered; (2) shock to a small area of brain passed off; (3) some edema cleared (edema comes after a little thrombosis and can clear); (4) collateral circulation may have opened up; (5) impulses in the brain may have been rerouted around the area destroyed. I doubt if one can expect much more improvement in a patient's condition after six or nine months have passed.

That most of the disability on the first day is due only to shock or edema is suggested by the report of Henry I. Russek and associates[6] to the effect that sudden and remarkable improvement has been seen after the prompt administration of cortisone. When the treatment was stopped in two cases, the paralysis returned, to disappear again when the use of the drug was resumed. I have no faith in injections of the stellate ganglion; first, because physiologists agree that such injections do not greatly dilate the arteries of the brain, if they dilate them at all; and second, because even if the vessels were to be dilated for about a half hour, I cannot see what good that could do after a thrombus has become well stuck in one spot and the resulting lack of blood has led to the complete and permanent destruction of a bit of the brain.

The patient who has had a little stroke always fears that he will soon have another, but I have seen many of these patients who went for 10 or 15 years without any more strokes that could be recognized. I usually prescribe one or two tablets of iodobrassid (Lipoiodine) to be taken daily. Sometimes, with its use, recovery has come even after several months of no improvement. Dr. John Gofman[7] has found that giving 3 grains (0.20 gm.) of thyroid substance daily tends to reduce greatly the amount

6. Russek, H. I., and others: Cortisone as an Adjunct in the Rehabilitation of the Hemiplegic Patient, Am. J. M. Sc. **225**: 147, 1953. Russek, H. I.; Zohman, B. L., and Russek, A. S.: Cortisone in the Immediate Therapy of Apoplectic Stroke, J. Am. Geriatrics Soc. **2**: 216, 1954.

7. Gofman, J.: Personal communication to the author.

of large molecule cholesterol in the blood, and this might help. The prognosis largely depends, of course, on how much of the brain has been destroyed. I am always most pessimistic about the persons whose character and ability have been badly changed for the worse. I cannot remember when I have seen such a person recover well. In many cases the prognosis must be guarded because no one can say when more strokes will come. I can tell patients that I have seen many persons go for 10 or 15 years in good health before another little stroke occurred.

Should one tell the patient that he has had a little stroke? I think it wise to discuss the possibility that there has been a little stroke, if only because so many of these people have a good hunch as to what happened to them the day they suddenly felt ill. This being true, they can hardly think much of the ability or frankness of the doctor who does not seem even to suspect what they had and why they have remained so long disabled, miserable, and unable to work. When the doctor and the family refuse to mention little strokes, the patient feels all the more frightened, isolated, and deserted. Most such persons whom I have seen have welcomed the chance to discuss their problems and fears. They were anxious to get answers to their questions, and, hence, they were glad that I was frank. Commonly, in such cases, I begin by asking "What did you think you were having that day when you had that dizzy spell and nearly fell down?" Often the patient says, "I thought I was having a stroke; I thought I was dying." Others, when asked if they ever had anything like a stroke, said, frankly and without any obvious concern, that they didn't think so. Only once during the last 30 years have I had a patient, a woman, who was upset by my opinion; so upset in fact that later she wrote and asked me to make another, more pleasant, diagnosis.

Physicians who believe in the theory of spasm of arteries can, of course, soften the blow to the patient and to the family by expressing the hope that all that happened was a temporary spasm. Often it is helpful to tell the patient that he need not fear that a third stroke will kill; this is only an old folklore with no truth in it. I tell my patients of some of the many persons I have seen who, after a stroke, became remarkably well. I may tell of Pasteur who, for 27 years after his big stroke, did much of his best work. Interestingly, his barber told a friend of mine, in Paris, that through the years Pasteur must have had 50 little strokes. I like to tell the family of the patient something about the little strokes, so that they can then be more understanding and more forgiving of the patient's cantankerousness or constant complaining. I tell them that the trouble is due to serious illness. So often the man becomes so irascible, unreasonable, and unkind that the family needs to know that the brain has been badly injured, and, because of this, he is a changeling. Also, if the family understands the real nature of the illness, they will not easily consent to futile operations on the brain or on the abdomen. The physicians must always be kind to those persons who have had a little stroke and must try to take good care of them. Some patients can be helped a great deal: many need help with insomnia; some need help with severe pain; and some, with Parkinson's disease, need special help with their rigidity and their tremor. Those who are mentally upset may need sanatorium care, and those few who are confined to bed need physiotherapy and rehabilitation.

In many cases a man's employers or partners need to know quickly that he is never likely to work again. Then they can retire him with a pension. Many a man who has lost his drive and skills should be retired quickly, before he wrecks the morale of the department. This is often a tremendous problem in business firms. Often, when a man owns his own business, the family ought to know that he is not likely to ever be of any use in the office. They must then decide quickly what is to be done with the business and the people who work there. To show what a physician often needs to do in these cases: a man of 55 years, with his three sons, had for years done well with a factory making women's dresses. He suddenly lost his old business ability and good sense and actually refused to let the designers bring out new styles. Naturally, in two years he had wrecked the business. His sons, baffled, exasperated, and unable to sell the out-dated product of the factory, quarreled with their father and left him. The minute I saw the man, with his dull face and his slowed-up mind, I drew from his wife the story of a pretty big stroke without paralysis or aphasia. When I got the patient to see what had happened to him, I talked him into turning the business entirely over to his sons, and then I talked them into coming back. Within a year they had the factory in production again.

SUMMARY

In millions of cases little thromboses in the brain slowly, over the course of 10 or 15 years, pull a person down, slow him up, age him, and eventually kill him. Unfortunately, unless the physician suspects the nature of the patient's trouble and asks about a sudden dizzy or woozy spell or a momentary blackout, the diagnosis will probably be missed. Because of the sudden pains that, with a little stroke, often shoot down into the thorax or abdomen, a tentative diagnosis of a coronary attack or carcinoma is often made.

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The Third Sex.—There is a third sex existent in our society today. This so-called "neutral gender" may be considered to encompass roughly all persons who have reached an average age of 60. . . . Long-range sex steroid replacement is the attempt to develop happier, better adjusted, more useful members of the "neutral gender," while they live out their increasing life span. There is no evidence to suggest, nor has any claim been made that steroid replacement increases longevity. Adequate, well controlled, sex steroid replacement however, can provide significant physical and psychic stimulation in the "neutral gender" age groups. . . . What is the present approach to sex steroid replacement in the neutral gender? In essence it is an attempt to treat the individual members of the third sex from a bisexual point of view. Advantage is taken of the state of essential castration associated with the third sex. Both of the individual sex steroids are used in combination rather than individually. Through combined therapy, every effort is exerted to avoid the untoward effects occasioned by either hormone when given individually or in a so-called "unopposed" manner. With the ratio of 20 to 1 (in milligrams) testosterone over estrogen, most of the criteria for combined therapy are met.—W. H. Masters, M.D., and J. W. Ballew, M.D., The Third Sex, *Geriatrics*, January, 1955.

PERSISTENT NASAL SYMPTOMS IN CHILDREN

CHAIRMAN'S ADDRESS

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The "problem nose" child, as defined for this study, has chronic nasal symptoms persisting longer than three months; however, all problem nose children do not necessarily fall into this category. According to the terminology used, a problem nose child is one who has persistent nasal symptoms, such as discharge, obstruction, sneezing, or general symptoms as bronchitis, cough, low grade fever, and fatigue. These children are seen by physicians in everyday practice, but are not always considered as problems because the majority of them are not seriously ill. To the parent of the child with persistent nasal symptoms a problem does exist, and it is the physicians' duty to diagnose and relieve this child of the symptoms. Physicians know these nasal symptoms are due to infection, allergy, systemic condition, foreign bodies, or abnormalities in the nasal passages.

Griffith [1] studied 5,000 patients who were sent to the hospital for removal of tonsils and adenoids and had various nasal complaints and grouped them under the following four types: (1) nasal, with constant nasal catarrh, general good health, and occasional sore throat and snoring; (2) general, with occasional vague headaches, fever often of unknown origin, mental dulness between attacks, and a muddy pasty complexion; (3) pulmonary, with recurrent bronchitis, tubercular suspects, intractable cough, and lowering of general health; and (4) referred, with disease in organs distant from the infection, such as rheumatism or nephritis. Types 2 and 4 are of infectious origin and types 1 and 3 allergic, infectious, or both. There may be many more symptoms than those mentioned above. Brown [2] discussed 50 symptoms occurring in children with chronic sinusitis and in a previous article [3] called attention to the similarity of symptoms in the prerheumatic child and one with chronic sinusitis. Among the systemic symptoms mentioned are anorexia, failure to gain weight, nausea, mild fever, aches, fatigue, headaches, night terrors, apathy, pallor, abdominal pain, nervousness, restlessness, enuresis, and frequent upper respiratory infection. The severity of the symptoms will vary with the virulence of the organism and the resistance of the patient. Cough, especially on reclining, is the most common symptom. Nasal or postnasal discharge is always present but may not be noticed.

Positive nasal findings should not be expected at all times. Frequent examinations may be required to determine the average appearance of the nasal cavity. The mucous membrane may vary from pale, boggy, and wet to hyperemic and dry. One or both sides may be obstructed, and, at times, both are open. A discharge may be seen in the nose. After the nose is inspected, material should be obtained, when possible, for microscopic examination and culture. The nasal mucosa should then be shrunken and the nasal cavity reexamined. It is not uncommon to have nasal pathology and no clinical evidence in the nose. Many of these "problem noses" are not detected on casual observation, and others are evident from a distance. Mollison and Kendall [4] reported evidence of sinus infection in 22% of 102 patients admitted for routine removal of tonsils and adenoids. Crooks and Signy,[5] 24%; Gerrie,[6] in 300 cases, 29%; White [7] checked 50 children admitted to the hospital for removal of tonsils and adenoids, and 41 had sinus diseases. These percentages are rather constant, but Birrell [8] gave such contrasting figures even in those children suspected of having sinusitis that Mawson and Gray [9] repeated the investigation of antral infections in unsuspected routine cases of patients admitted for removal of tonsils and adenoids to see if Birrell's percentages or those given by others were correct. Meticulous care was taken to prevent any mistakes, and a double cannular-aspirating technique was used to prevent contamination of antral contents from any organism that might be in the nasal cavity. The instance of unsuspected pathological infection in a series of 50 cases was 22%, about the same as previously reported and in agreement with the findings of other investigators previously mentioned.

From these reports it is justifiable to conclude that the referring physicians paid little attention to the nasal condition when the tonsils and adenoids were present or were suspected of being the cause of the nasal symptoms and removal was advised for relief of the nasal symptoms. Griffith [1] studied 385 patients with nasal complaints who had tonsils and adenoids removed, with no improvement or nasal symptoms made worse. Looper [10] was impressed with his frequent encounter with children who had their tonsils and adenoids removed with no desired results and advised paying more attention to the nasal symptoms before removing the tonsils and adenoids. Certainly these studies emphasize the necessity of a thorough nose and throat examination before a child's tonsils and adenoids are condemned. An inspection of the nose is not a thorough examination. A good history, examination of the nasal cavity before and after shrinkage and when nasal disease is suspected, roentgenograms, nasal smears,

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Read before the Section on Laryngology, Otology and Rhinology at the 103rd Annual Meeting of the American Medical Association, San Francisco, June 24, 1954.

1. Griffith, I.: Function of Tonsils and Their Relation to Etiology and Treatment of Nasal Catarrh, Lancet **2**: 723-792 (Sept. 25) 1937.

2. Brown, E. E.: Fifty Symptoms of Chronic Sinusitis in Children with Differential Diagnosis of Each Symptom, Arch. Pediat. **67**: 553-556 (Dec.) 1950.

3. Brown, E. E.: Sinusitis and the Prerheumatic Child, Arch. Pediat. **67**: 354-357 (Aug.) 1950.

4. Mollison, W. M., and Kendall, N. E.: Frequency of Antral Infection in Children, Guy's Hosp. Rep. **72**: 225-228 (April) 1922.

5. Crooks, J., and Signy, A. G.: Accessory Nasal Sinusitis in Childhood, with Records of Bacterial Examinations, Arch. Dis. Childhood **11**: 281-306 (Dec.) 1936.

6. Gerrie, J.: Nasal Sinusitis in Children, Brit. M. J. **2**: 364, 1939.

7. White, F. W.: Pathologic Nasal Accessory Sinuses in Children, Ann. Otol. Rhin. & Laryng. **30**: 221-227 (March) 1921.

8. Birrell, J. F.: Chronic Maxillary Sinusitis in Children, Arch. Dis. Childhood **27**: 1-9 (Feb.) 1952.

9. Mawson, S., and Gray, J. D.: Incidence of Chronic Infection of the Maxillary Sinus in Children, J. Laryng. & Otol. **67**: 556-566 (Sept.) 1953.

10. Looper, E. A.: Infection of Nasal Accessory Sinuses in Children, M. Clin. North America **21**: 1323-1334 (Sept.) 1937.

and cultures are necessary. The adenoids should be inspected as well as the other lymphoid structures in the throat. The condition of the adenoids and other lymphoid structures should be considered in evaluating the nasal condition. Adenoids are prone to return when removed from persons with allergies unless the allergy is controlled.

DIAGNOSTIC PROCEDURES

The value of roentgenograms of sinuses of children is questionable, but with proper technique much information can be obtained. Some radiologists or their technicians do not obtain good plates on children, but it can be done with patience and perseverance. The otolaryngologist should not have to depend on the radiologist to interpret the films. The clinician has an advantage over the radiologist in knowing the history and findings in the nose. Those otolaryngologists who have roentgenograms made of all cases of suspected sinus involvement seem to appreciate their value more than those who occasionally request a roentgenogram. The rhinologist who is capable of making roentgenograms feels there is a distinct advantage in having these facilities convenient, for it is often necessary to make pictures with minor variations of exposure and position to bring out the suspected changes in the sinuses.

The examination of nasal secretion is another diagnostic procedure of value. The gross appearance of the discharge in the nose is misleading. Some mucoid material is void of eosinophils and contains many bacteria. What grossly appears to be pus on microscopic examination may show many eosinophils. Eosinophils are present in the reparative phase of chronic infection but not in large numbers. An idea can be obtained of the kind and number of bacteria. There is also information to be determined from the study of the epithelial cells. The value of the study of the nasal secretion is sometimes questioned, and some physicians may say it is not needed for a diagnosis. Any proof to sustain these suspicions are convincing, and all available information is needed in many cases.

Much information can be obtained from a nasal culture. Dr. Goldman [11] and others have shown that pathogenic bacteria are not routinely found in a normal nose. Smears taken from the middle meatus are void of pathogenic organisms unless there is an infection in the nose. This does not hold true in the nasopharynx. Blood agar plates may be inoculated, and if a growth is obtained its sensitivity to the various antimicrobials can be tested. With this information the most effective antimicrobial can be prescribed. Many physicians believe that nasal cultures or sensitivity tests are too expensive to have performed, but the cost to the patient is less than the usual prescription for an antimicrobial, and when it is necessary to switch from one antimicrobial to another, the expense to the patient is greater in time and money than it would have been for the sensitivity test and the prescription for a proper antimicrobial.

These procedures seem technical and complicated, but actually a busy practitioner can carry them out with a little equipment and instruction. I believe more physicians would take advantage of these diagnostic procedures in some, if not all cases, if they realized the simplicity of performing them. The day is fast approaching when all physicians will have to know the sensitivity of the infecting organism to the antimicrobial prescribed if they expect to get results. The bacteria are becoming resistant to antimicrobials because of their frequent and promiscuous use.

ALLERGIES

Allergy must be differentiated from infection. Allergies play a major role in the production of nasal symptoms in children. A good history is essential in making any diagnosis; in allergy it is a necessity. The possibility of allergy in the family should be investigated. The appearance of colic, skin rashes, eczemas, and disturbances when new foods are added to the diet suggests allergy. The runny or itchy nose, sneezing when exposed to temperature changes, hacking cough, recurrent attacks of bronchitis, asthma, fatigue, transitory involvement of hearing, pallor, or other general symptoms may also be present. The child with symptoms of allergies is seldom sick, but his parents worry about his persistent or recurring symptoms, especially the discharge from his nose.

Nasal Findings.—Although the nose affected by allergies is supposed to have a pale, glistening, edematous mucous membrane there may be many variations. A thin, watery or mucoid nasal discharge and varying degrees of obstruction of the nose are usually present. In the child with allergies affecting the nose, the sinuses are usually clear on x-ray. If any change in density is present it is usually uniform in all sinuses. There is a preponderance of eosinophils and neutrophils in the nasal smear. There are no pathogenic organisms on culture.

Skin Tests.—Offending agents are not hard to isolate in children. For instance if symptoms are seasonable, pollens are suspected; if perennial, house dust, Alternaria, Hormodendrum, or foods. When the child is less sensitive to house dust, symptoms may only be present in winter. It is not necessary to perform many skin tests on a child, only enough to confirm suspicion of sensitivity. In my opinion skin tests are not reliable in infants. In interpreting the skin test, the age of the patient, the reactivity of skin, and the strength and reacting properties of the testing solution should be kept in mind.

Treatment.—To treat the child with allergies, offending foods should be eliminated. Hyposensitization to inhalants and pollens should be accomplished. In hyposensitization, a search is made for the dose that gives the patient relief from his symptoms for the longest period of time, and when that dose is determined it should be given as indicated.

Truth About Common Misconceptions of Allergy.—A child will not outgrow his allergy. The infantile eczema will disappear, but the child is likely to have asthma around the age of puberty, which indicates a change in the shock organs and not an outgrowth of allergy. Hundreds of skin tests are not necessary to make a diagnosis in allergy. A good history, knowledge of a patient's likes and dislikes and eating and other habits should reduce tests to a minimum. Some allergists only perform skin tests for inhalants, pollens, and common foods. Some

11. Goldman, J. L.: Bacteriological and Clinical Interpretation of the Flora of the Nose and Nasopharynx in Adults, Ann. Otol. Rhin. & Laryng. **59**: 156-165 (March) 1950.

have even discarded food tests. Allergy is not a new fad only for rich persons. It is found in all levels of life. It was recognized and mentioned in early medical writings.

SINUS INFECTION

The severity of the symptoms from infection will vary with the resistance of the patient and virulence of the organism. Chronic sinus infection in children does not necessarily result from an acute infection, as in adults. The onset may be insidious. Among the more common symptoms are bad breath, postnasal or nasal discharge, morning nausea or vomiting, cough especially on reclining, bronchitis, elevation of temperature, aching, fatigue, night terrors, anorexia, abdominal pain, recurrent upper respiratory infection, and headaches usually of a vague character.

Nasal Findings.—The skin of the nostril may be raw or crusty in infection. The mucous membrane may be hyperemic and the turbinates congested on one or both sides. Purulent or mucopurulent discharge may be seen in the nose. The nose may show no clinical findings to indicate infection is present. Tenderness over the maxillary sinus is very rare, but may be present in the acute frontal or ethmoid. The nasopharynx may show the presence of adenoids. Varying degrees of density and thickening of the lining mucosa in the involved sinuses can be seen on roentgenograms. Smears show a preponderance of bacteria, pus cells, and very few if any eosinophils. Cultures will be positive for pathogenic organisms.

Treatment.—The principles of treatment are adequate drainage, drugs, and the elimination of infecting organisms by building up the patient's resistance. To have proper drainage the ciliated epithelium in the nose and sinuses must function and the ostia of the sinuses remain open. Shrinkage of the tissue around the ostia by local treatment is beneficial. Displacement has its advocates. When the antrum does not empty, irrigation must be made through the natural ostium or inferior meatus by means of a trochar. If systemic medication and irrigation does not accomplish results, a nasoantral window is indicated.

After determining the infecting organism and its sensitivity, the proper antimicrobial, if tolerated, should be prescribed in large enough doses and over a long enough period of time to kill the infection. Vitamin B complex should be given with all mycins, and vaccines should then be used, as apparently the necessary antibiotics to resist future infections after antimicrobials are administered are not building up. Medicaments to shrink the nasal mucosa and establish breathing space are helpful, but those containing antibiotics should be avoided because of the possibility of sensitizing the patient and because of their questionable local benefit. In my experience naphazoline (Privine) hydrochloride should be avoided because of its damaging effects to the nasal mucosa when used over an extended period. If prescribed the prescription should be marked *non repitor.*

Adequate rest, balanced diet, and vaccines are indicated to build up body resistance. Some radiologists have reported excellent results with roentgenographic therapy in children with so-called "sino bronchitis." My experience in this type of therapy has not been gratifying. Radiation therapy is based on the theory that "the disintegration of the hypertrophied lymphoid elements of the hypertrophic membrane and lymphocytes, which liberate bacterio lysins thus stimulating the microphages to greater activity and reduction of edema of the sinus ostia promoting free drainage and aeration."[12]

Truth About Common Misconceptions of Sinus Infection.—If the sinus is irrigated the procedure will not have to be continued indefinitely. Irrigation of the sinuses, regardless of the method used, has no injurious effect on the sinuses. Once a sinus is infected it will not always remain so. The sinuses are practically always involved when symptoms of infections in the nose are present over a week. Many sinus infections clear up spontaneously. Like infection anywhere else in the body, if treated early it is less likely to become chronic. It is commonly believed that a cold if treated will last 14 days, if untreated two weeks. What is a cold? To the layman and many physicians a cold is anything that produces nasal symptoms, such as allergies, acute sinus infections, exacerbations of chronic sinus infection, and virus infection. To the rhinologist a cold is a specific entity, probably caused by Dochez's filtrable virus. The Bryans[13] using a modification of Papanicolaou's stain observed a characteristic pattern of nuclea cytoplasmic degeneration in the ciliated epithelial cells in the nasal secretions of patients with common colds. This pattern was not found in allergic, radiation reaction, or subacute or chronic sinus infection. This important discovery can now be used as a differential diagnostic procedure when indicated.

Nasoantral windows do not necessarily close up rapidly in children, if precautions are taken to prevent unnecessary trauma, such as the use of small instruments, fracturing the inferior turbinates toward the septum to prevent injury to the mucous membrane on the lateral aspect of the turbinate. If a large opening is made in the nasoantral wall and care taken to bite the edge of the mucous membrane off sharp and smooth with the bone to prevent strings of tissue forming bands of adhesions, if the turbinate is packed towards the septum, and if the opening is cannulized after removal of the packing, the window will remain open in most cases.

Surgical procedures on the sinuses are satisfactory, and one operation does not necessarily call for another. Surgery is done to establish drainage or remove diseased tissue. The logical reasons for the misconception that it is not satisfactory are: 1. There are eight sinuses, and, if all are bad, attacking one surgically or even three, as is often done in one operation, will not cure all eight. When surgery is necessary at least two procedures would be required. 2. Allergy was not differentiated from infection when so much sinus surgery was being done. More has been learned about allergy, and it is now known that allergic sinusitis will respond to allergy management.

CAUSES OF "PROBLEM NOSES"

Many general conditions play a part in the production of a "problem nose" child. A preponderance of lymphoid tissue, hypothyroid, and other systemic symptoms sometimes produce a problem nose. Chubby children who

12. Butler, F. E., and Woolley, I. M.: Roentgen Therapy in Chronic Sinusitis: Further Report, Radiology **23**: 528-537 (Nov.) 1934.

13. Bryan, W. T. K., and Bryan, M. P.: Structural Changes in the Ciliated Epithelial Cells During the Common Cold, Tr. Am. Acad. Ophth. **57**: 297-302 (May-June) 1953.

usually come under the above headings may have a problem nose. Many of these are grouped under the vague and general term of vasomotor rhinitis. Some otolaryngologists consider vasomotor rhinitis as a disease entity, but ordinarily the term as used is about as specific as "red throat."

Occasionally one sees unusual occurrences, such as occlusion of the choana, rhinolites, and congenital deformities, that may produce nasal problems. The diagnosis is evident by examination. A deviated septum may occur from injury-producing symptoms that are relieved by correcting the deformity. The adenoids play an important part in nasal problems. They may obstruct or partially obstruct breathing or prevent adequate drainage from the nose. Mouth-breathing and snoring may result from such obstruction. The adenoids catch and hold secretions. These accumulations of secretions, which sometimes dry on the nasopharynx, play a part in producing morning nausea and sore throat. Remnants of the adenoids are especially prone to produce sore throats in the mornings or after dark. Adenoids removed from the child with allergies will return unless the allergy is controlled. When completely removed from children with infected sinuses the adenoids may not return, but often there is a hypertrophy of the lymphoid bands on the lateral wall of the pharynx, and sometimes a granular pharyngitis develops.

On first thought the mention of foreign bodies in the nasal passages as the cause of a "problem nose" seems foolish, but every otolaryngologist can recall patients with foreign bodies in their noses who have been treated for sinus trouble. My latest patient with a nasal foreign body had a piece of chewing gum in the nostril and had been treated a year for "sinus" by a specialist in another field. Because of this and similar cases I have tried to find out how much the physician with the average training can see in the nose. The results have been astounding. In the past year I have seen one medical student and only one intern, who on finishing his prescribed training could make a satisfactory nasal examination. In my association and conversation with allergists practically 90% admit they are not satisfied with their nasal examinations. I have seen two general practitioners who do a fair job of examining the nose.

If the number of doctors who cannot make a nasal examination are added to those in the speciality who do not have the time and patience necessary to examine and treat children, it can easily be seen that many children with nasal symptoms will continue without a diagnosis. Every patient with nasal symptoms should have a definite diagnosis with the cause of the symptoms determined. The treatment of symptoms, that is, prescribing of antihistamines and antimicrobials without attempting to make a definite diagnosis is unwarranted and, in my opinion, is one reason there are so many "problem nose" children.

CONCLUSIONS

All children with nasal symptoms should have a thorough nose and throat examination. Differentiating allergy from infection in all nasal cases is essential. A thorough nasal examination should be performed before removal of tonsils and adenoids. Removal of tonsils and adenoids should not be expected to clear up nasal symptoms. The prescribing of antihistamines and antimicrobials without a diagnosis should be discouraged. More time and thought should be given to the instructions of the medical students and interns in the field of rhinology.

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CLINICAL NOTES

A COMPARATIVE CLINICAL STUDY OF SEVERAL ENEMAS

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The use of solutions to cleanse the lower intestine (enema, clyster) dates back to the dawn of recorded history. Lieberman [1] points out that some of the earliest references to enemas are found in the cuneiform inscriptions on Babylonian and Assyrian tablets (ca. 600 B. C.). Celsus (25 B. C.-50 A. D.) gave an exact description as to when and how to administer an enema. He used sodium chloride solution or sea-water enemas to remove "excreta accumulated near the exit." Avicenna (980-1037 A. D.) is credited with the introduction of the "clyster-purse" or collapsible portion of an enema outfit made from ox skin or silk cloth and emptied by squeezing with the hands. The popularity of enemas has varied from era to era, the 18th century apparently marking a particularly low point in their extent of use. Today, however, the value of a satisfactory enema solution properly used is well nigh universally recognized as a desirable procedure for a variety of purposes. A search of the literature fails to reveal any studies directed to a comparison of various enemas. Incident to the introduction of a new disposable enema unit, opportunity was had to determine its effectiveness and that of the older commonly used enemas of sodium chloride solution, soap suds, and tap water. As subjects, 10 male medical students, 22 to 26 years of age, were used. All subjects had suffered from chronic constipation for several years, having hard stools at intervals of two to five days. The subjects were free of any gastrointestinal disease.

TECHNIQUE AND MATERIALS

The four enemas used were (1) Fleet enema disposable unit, (2) sodium chloride solution, (3) soap suds, and (4) tap water. The Fleet enema solution is contained in a 4.5 oz. plastic compressible dispenser, each 100 cc. of solution containing 16 gm. of sodium biphosphate and 6 gm. of sodium phosphate. The sodium chloride solution

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This study was supported by a grant from the C. B. Fleet Company, Lynchburg, Va.

1. Lieberman, W.: The Enema: Some Historical Notes, Rev. Gastroenterol. 13: 215-229 (May-June) 1946.

enema was made by dissolving two teaspoonfuls of sodium chloride in 1 qt. (946 cc.) of tap water. Soap suds enema was made after the usual manner by working a cake of soap around in tap water until the solution was

can, with length of rubber tubing and a hard rubber tip attached, was used to deliver the three conventional types of enema. They were given by the gravity method, with the enema can being elevated 12 to 18 in. above the level

Differences in Time Required for Enema Procedures

Enema	Subject No.	Age	Weight, Kg.	Time to Prepare Enema		Time to Instill Enema		Time of Retention in Knee-Chest Position, Min.	Time to Evacuate, Min.	Total Time of Administration, Retention, and Evacuation	
				Min.	Sec.	Min.	Sec.			Min.	Sec.
Fleet enema disposable unit	1	23	70.8	..	..	0	10	2	5¼	..	..
	2	23	70.3	..	..	0	10	4	5¼	..	..
	3	26	83.0	..	..	0	10	4¼	5½	..	..
	4	24	77.1	..	..	0	10	3½	9½	..	..
	5	23	63.5	..	..	0	9	5	5¼	..	..
	6	23	78.9	..	..	0	10	6½	4¾	..	..
	7	22	77.1	..	..	0	11	4½	3	..	..
	8	22	55.4	..	..	0	9	4	5	..	..
	9	22	58.1	..	..	0	9	14*	6	..	..
	10	22	75.3	..	..	0	10	3	3	..	..
	Average	..	....	..	20	..	10	5	5¼	10	45
Water	1	..	....	..	..	1	30	7	10	..	..
	2	..	....	..	..	1	45	4½	4½	..	..
	3	..	....	..	..	1	30	11	15	..	..
	4	..	....	..	..	1	30	2¾	4½	..	..
	5	..	....	..	..	2	45	8¼	8	..	..
	6	..	....	..	..	2	0	5½	14	..	..
	7	..	....	..	..	1	30	8½	9	..	..
	8	..	....	..	..	1	5	3½	6	..	..
	9	..	....	..	..	2	0	5	9½	..	..
	10	..	....	..	..	1	5	4	10, 3†	..	..
	Average	..	....	2	0	1	34	6	9	18	34
Soap suds	1	..	....	..	..	1	30	8½	12½	..	..
	2	..	....	..	..	1	20	5	10	..	..
	3	..	....	..	..	1	30	10	20	..	..
	4	..	....	..	..	1	30	6½	17	..	..
	5	..	....	..	..	3	..	3	14	..	..
	6	..	....	..	..	1	30	8¾	12	..	..
	7	..	....	..	..	2	10	7	11	..	..
	8	..	....	..	..	1	30	4½	13	..	..
	9	..	....	..	..	1	5	8½	11¾	..	..
	10	..	....	..	..	2	15	5½	12, 5‡	..	..
	Average	..	....	3	0	1	43	6¼	14	24	58
Sodium chloride solution	1	..	....	..	..	1	30	18*	26	..	..
	2	..	....	..	..	1	30	6¾	5, 5§	..	..
	3	..	....	..	..	2	0	15	33	..	..
	4	..	....	..	..	2	45	17*	25	..	..
	5	..	....	..	..	2	15	6	6, 6, 7‖	..	..
	6	..	....	..	..	2	0	17*	18	..	..
	7	..	....	..	..	1	30	15*	9	..	..
	8	..	....	..	..	1	5	20*	8	..	..
	9	..	....	..	..	2	0	20*	15	..	..
	10	..	....	..	..	1	30	18*	16	..	..
	Average	..	....	4	0	1	48	15¼	17½	38	33

* As no peristaltic rush had taken place the "wait" in the knee-chest position was arbitrarily terminated.

† After an initial waiting period on the stool for 10 minutes, a mass of feces and fluid was seen. A clear view was noted after an additional wait of three minutes.

‡ Immediately on passing the sigmoidoscope, a peristaltic rush was met containing feces and fluid. After a second wait on the stool for five minutes 2+ feces were seen at a level of about 15 cm.

§ After an initial waiting period of five minutes on the stool, sigmoidoscopic examination showed 3+ feces. After five more minutes on the stool, the sigmoidoscope was again passed and 1+ feces noted along the entire length of view.

‖ After the first waiting period of six minutes on the stool, approximately 4 fluid ounces (120 ml.) of fecal-tinged fluid ran out and 3+ feces obliterated proper sigmoidoscopic viewing. After a wait of six additional minutes 3+ feces was still seen. After a third wait of seven additional minutes 2+ feces were seen through the sigmoidoscope. Subject still felt need of bowel movement for 5 additional minutes with uncomfortable peristaltic rushes and passage of gas for 40 minutes.

notably opaque and frothy. Tap water enema required no added ingredients. Fleet enema solution was given in the volume of about 4.5 fluid ounces (133 cc.) at a temperature of 26 C and the other enemas in 1 qt. quantities at body temperature. The usual apparatus of enema

of the anus. The Fleet enema solution was administered by squeezing the contents from its compressible container. All enemas were given with the subjects in knee-chest position, and this position was maintained until the urge to evacuate occurred.

The intestinal mucosa was viewed with a sigmoidoscope before and after each enema and a comparison made of the cleansing effect and any other changes such as hyperemia, spasm, bleeding, and the presence of mucus. In evaluating the degree of cleansing afforded by the enema an arbitrary grading of from zero (clean mucosa and lumen without any signs of feces or fluid) to 3+ (signifying that proper viewing of the intestinal lumen with the sigmoidoscope was prevented by much feces filling the lumen and lining the walls of the intestine) was used. Similarly, an arbitrary grading of from zero to 3 was used in reference to the degree of mucus, hyperemia, spasm, and bleeding observed. In all of the preenema sigmoidoscopic views fecal masses were seen but no abnormal findings noted. Each of the subjects received all four of the enemas described, with an interval of two to eight days between enemas. Each subject was observed for any adverse effects during administration, retention, and evacuation and for any "after-effects." Also the time required in preparation of enemas, time consumed in administration, time of enema retention, and its evacuation were noted.

RESULTS

The table indicates the differences in times required for the procedures, and it can be seen that the Fleet enema required less time to prepare (averaging 20 seconds), less time to instill (averaging 10 seconds), less time of retention (averaging 5 minutes), less time for evacuation (averaging 5¼ minutes), and no time was necessary to clean and store the disposable unit. The total time required to complete an enema using this unit was, on the average, 10 minutes 45 seconds, as compared with water (averaging 18 minutes 34 seconds), soap suds (averaging 24 minutes 58 seconds), and sodium chloride solution (averaging 38 minutes 33 seconds). In the postenema sigmoidoscopic examination it was seen that the Fleet enema afforded 7 out of 10 completely clean sigmoidoscopic fields. The remaining three subjects were graded 1+, indicating that a few flecks of feces were seen in two instances and a small amount of fluid in the third case.

The plain water enema provided 3 out of 10 completely clean sigmoidoscopic views. There were three instances of 1+ feces and four instances of 3+ feces. With soap suds enema there were four instances of completely clean sigmoidoscopic fields, three instances of 1+ feces, and three instances of 2+ feces. With sodium chloride solution enema there was only one instance in which the sigmoidoscopic field of vision was completely clean, five instances of 1+ feces, one instance of 2+ feces, and three instances of 3+ feces. Mucus was rarely encountered, being seen in two subjects with the use of the Fleet enema and once each with water and soap suds. The mucus seen was thin and watery and did not interfere with satisfactory visualization of the intestine. Hyperemia was noted in one case in a subject using a plain water enema. Spasm, of a mild degree, (graded 1+), was observed in one subject using soap suds enema. In two subjects using sodium chloride solution enemas moderate spasm (graded 2+) was noted.

PARAPLEGIA RESULTING FROM SEVERE KYPHOSCOLIOSIS

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Kyphoscoliosis is a common deformity of the spine, and, although it may be associated with other conditions that involve the spinal cord, such as tuberculous granuloma or a tumor,[1] the deformity of the spine itself is seldom the cause of the neurological disturbance. On occasion, however, the kyphoscoliosis and the distortion of the dura mater accompanying it may so compress the spinal cord as to produce a paralysis below the level of the compression. This may happen years after the kyphoscoliosis first appeared. It is important that the possibility of such a disorder be recognized and that the condition is generally correctible with proper surgical treatment. The importance of the proper management of the condition was first emphasized by McKenzie in 1927 [2] when he reported a case treated with laminectomy and incision of the dura mater. He stated that he had been encouraged by the good results obtained by Sachs [3] in a similar case. Paraplegia resulting from a scoliosis was recognized early by Macewen in 1888,[4] but a complete review of the condition was not made until 1949 by McKenzie and Dewar.[5] In the majority of the cases the paraplegia was found to occur at the period of most rapid growth, e. g., between the ages of 12 and 19 years. The oldest patient reported in the literature is 43 years old.[6] It is of special interest that in the patient to be discussed here the symptoms of paraplegia did not appear until the age of 58 years, although the scoliosis dated from early childhood.

REPORT OF A CASE

A 61-year-old man was first admitted to the neurosurgical service at the Chicago Memorial Hospital on Jan. 23, 1950, with the following history. At the age of 4 years the patient fell from a stairway and fractured his neck. His neck was immobilized for some time thereafter. He recalled no paralysis at that time. At the age of 11 he fell off an icebox, injuring his left arm, and shortly after the fall he noticed a weakness and atrophy of the left forearm and hand. Otherwise he was in good health until June, 1948, when he began to note tingling sensations in the toes of both feet and cramps and twitching of the calf muscles. In the fall of 1948 he noticed an unsteadiness when he was on his feet, particularly after arising from the lying or sitting positions. In March, 1949, the patient was seen elsewhere. The examination at that time revealed spasticity and slight weak-

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ness in both legs with bilateral Babinski signs and atrophy of the thenar eminence of the left hand with paralysis of the flexors of the left index finger. There was no sensory disturbance. A lumbar puncture showed a partial block and 80 mg. of protein per 100 cc. of fluid. In April, 1949, a myelogram at the other clinic failed to reveal any tumor. His condition remained stationary up until six weeks before his admission to Chicago Memorial Hospital when he began to note a steady decrease in the strength of both legs, particularly the left. He had had mild hesitancy in starting the urinary stream for several years. He complained of transitory urinary retention following the myelogram in 1949.

The patient had gonorrhea in 1910 and a meatotomy in 1924 followed by cystitis. He had had poor hearing on the right since otitis media 30 years before. A basal cell carcinoma was removed from the apex of the left ear in 1949. General physical examination revealed a well-nourished man. He had a short neck, with marked limitation of movement in all directions. There was a marked kyphoscoliosis of the lower cervical and upper thoracic spine with a convexity toward the left. He had bilateral inguinal hernias, more pronounced on the right. The blood pressure was 150/90 mm. Hg, pulse 80, and temperature 97.6 F.

Neurological Examination.—Examination of the cranial nerves revealed slight conduction-type deafness on the right. The sensory examination showed hypalgesia in the distribution of the ulnar nerve on the left side; other than this there was no sensory impairment. There was atrophy and weakness of the intrinsic muscles of the left hand. He was unable to flex his left index finger completely. In the lower extremities he had moderate weakness of both quadriceps extensors and hamstring muscles bilaterally. There was marked weakness of dorsiflexion of the left foot and weakness of eversion of both feet. The abdominal reflexes were absent. There was spasticity and hyperreflexia in the lower extremities. Babinski's sign was present bilaterally.

Laboratory and X-Ray Examination.—The blood cell count and urinalysis were normal. The blood Wassermann and Kahn tests were negative. X-ray examination of the chest showed slight enlargement of the heart and widening and tortuosity of the dorsal aorta. Preoperative films of the upper spine revealed marked scoliosis of the upper five thoracic vertebrae toward the left, with much deformity of the fifth, sixth, and seventh cervical and first thoracic vertebrae, resulting in a posterior bowing at the cervicothoracic junction and narrowing of the posterior diameter of the spinal canal at this level (see figure). The impression was that he was suffering from a cervicothoracic kyphoscoliosis with compression of the spinal cord. The exact origin of the scoliosis was not definite. Although there was a history of trauma, the x-ray examination revealed sufficient destruction of the vertebral bodies to suggest the possibility of an old tuberculous lesion. A laminectomy for relief of this compression was decided upon.

Operative Procedure.—On Jan. 9, 1950, a long, curved incision parallel to the scoliosis was made in the midline of the back of the neck and upper thoracic region. The muscles were separated from the spinous processes and laminas from the second cervical to the fourth thoracic vertebrae. The spinous processes and laminas were removed from the upper three thoracic vertebrae and from several lower cervical vertebrae. The exact ones could not be positively identified, but the operator believed that the delamination extended from the fourth cervical vertebra downward. The spinal canal followed a most tortuous course. Going from below upward, it began to the left of the midline at the level of the third thoracic vertebra and then curved gently upward and toward the right side until it reached about the fifth or sixth cervical vertebra, where the canal turned sharply toward the left and backward. Difficulty was encountered in delaminating the vertebrae at this point because of the extremely sharp angle. The dura mater in the cervical region was thickened to approximately 2 mm., particularly on the right side. Elsewhere it appeared normal. When the dura mater was incised longitudinally the edge separated, revealing an elliptical opening, but the dura mater on the right side was still taut and compressed the spinal cord. Then transverse incisions were made in the dura mater on the right side. These spread into wide V's completely releasing the tension on the dura mater and the compression of the spinal cord. No granuloma or neoplasm was seen anywhere, and the spinal cord did not appear to be compressed by any bony structure. At the close of the operation the cord seemed perfectly free, although still tortuous, and it pulsated freely. The dura mater was left open, and the soft tissues of the back were closed in layers with interrupted silk sutures.

Postoperatively the patient moved all extremities, and sensation was present as preoperatively. He had to be catheterized for about four days. He was up walking on the ninth postoperative day. About a week after the operation he began to complain of root pain in the left upper extremity. He was fitted with a cervical collar, but his arm pain remained. Gradually, the root pain in the left shoulder and arm improved. He was discharged on March 10. At this time he was able to walk more steadily and did not drag his left foot as much as he did preoperatively.

Second Admission.—The patient reentered the hospital on March 18, 1950. A few days before the admission he had felt that his left leg had become weaker, particularly in flexing the thigh at the hips. The day before the admission he began to have pain in the posterior aspect of the neck radiating into the superior and posterior aspects of the left shoulder. He did not have his old pain in the left hand. The neck pain was worse when the patient sat up or stood up. The examination revealed

A, anteroposterior view of cervicothoracic spine showing severe scoliosis with marked deformity of the lower cervical vertebra. *B*, oblique view of the cervicothoracic spine (taken postoperatively) showing severe kyphoscoliosis centering at the cervicothoracic junction with partial forward dislocation of the seventh cervical vertebra on the first thoracic.

marked limitation of motion in the neck due to pain. The neurological status was about the same as preoperatively, though there was perhaps some increase in the weakness of the left leg. Blood cell count and urinalysis were essentially normal. X-ray examination of the cervicodorsal spine showed the old kyphoscoliosis and evidence of extensive laminectomy but no significant new developments.

Halter traction was applied to the cervical spine with fairly good relief of the neck and shoulder pain. Ten days after the admission he again noticed root pain in the left arm and hand and still exhibited weakness of the left leg in walking. The strength of the left leg gradually decreased, and the patient's walking deteriorated; however, about the middle of May his gait began to improve and continued to do so. He complained mostly of steady root pain in the left arm and hand. This was still present at the time of his discharge, but his walking improved steadily. He was able to get around fairly well with a cane when he left the hospital on Aug. 5, 1950. Following his discharge from the hospital he was seen at regular intervals as an outpatient. On April 19, 1951, he was working regularly. His walking was almost normal, but he stated that his left leg tired easily. He still had pain in the ulnar area of the left forearm and hand. The examination revealed the same findings in the upper extremities. The reflexes in the lower extremities were not hyperactive at this time. The abdominal reflexes were present. There was no Babinski's sign. He was last seen on

May 22, 1954; at this time he was very happy with his physical condition. His only complaint was occasional pain, once every three or four months, in the ulnar distribution of the left arm. He was working full time and had no difficulty in walking. The examination revealed the old muscular weakness and atrophy in the left arm. The reflexes were normal. The gait was normal; he could hop on either foot alone. The x-ray examination of the cervicodorsal spine at this visit did not show any striking change from the ones made earlier.

COMMENT

The case reported demonstrates a typical instance in which paraplegia developed as a late complication of kyphoscoliosis and was successfully treated with laminectomy and incision of the dura mater. There is still some controversy about the management of these cases. Kleinberg [7] and Ridlon [8] reported cases that were improved with conservative treatment only. This usually consists of traction, body casts, and orthopedic frames. Since then Kleinberg and Kaplan [6] reported another case of paraplegia collected from the literature. Some workers have been treating the paraplegia with spinal fusion only. Ruhlin and Albert [9] reported one case that did not improve with fusion; on the other hand, Kerr [10] reported one case in which a complete recovery was accomplished with spinal fusion without a laminectomy. However, as Bucy and Heimburger [1] pointed out, traction and mechanical efforts to correct the spinal deformity may precipitate a paraplegia or aggravate an existing one. The location of the deformity, the duration of the symptoms, and the age of the patient play some part in the choice of the treatment. In the case reported, the patient's advanced age and history of scoliosis from early childhood and the location of the lesion made laminectomy with incision of the dura mater preferable. This decision is well supported by the gratifying results obtained following the operation. It should be noted that the laminectomy is not the important part of the surgical procedure. The compression of the spinal cord is usually from side to side and produced by the taut dura mater. The important part of the surgical procedure is the transverse incision of the dura mater and the release of this compression. It is also interesting to note that the condition of our patient deteriorated in the early postoperative period, but this was followed after a few months by a steady improvement. A similar course is observed in the case of a 43-year-old man reported by Kleinberg and Kaplan.[6]

SUMMARY AND CONCLUSIONS

A 61-year-old man developed a paraplegia some 54 years after he developed a severe kyphoscoliosis at the cervicothoracic junction. This was successfully treated by laminectomy and relaxing incisions of the dura mater.

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SPECIAL ARTICLE

PHYSIOLOGY AND FUNCTIONS OF THE WHITE BLOOD CELLS

THE MINOT LECTURE

John S. Lawrence, M.D., Los Angeles

It is both an honor and a pleasure to appear before you as the George R. Minot lecturer. It was my good fortune to know Dr. Minot over a period of many years. He afforded me an opportunity to do some experimental work in the Huntington Memorial Hospital in 1923 while I was waiting for my internship at the Massachusetts General Hospital. Later, I was to return to work under his general guidance in Thorndike Memorial Laboratory. He was, as is well known, interested in medicine in general and, in particular, in problems relating to the broad field of hematopoiesis. He emphasized constantly the fact that one could not study one of the morphological elements in the blood without considering the others. My special interest was at that time and has continued to be the white blood cells and their relation to the hematopoietic system and the body as a whole. For this reason, it has seemed to me pertinent to present a few of the more recent and current developments in this field with which this laboratory has been closely associated. This is not done with any intention of neglecting the valuable work coming from many sources throughout the world but is only due to the fact that I have felt that subjects with which I am closely associated could be more satisfactorily handled in the time available. With this in mind, most of this discussion will be concerned with the following topics: 1. Biochemical studies of the white blood cells. This program is under the supervision of Dr. William N. Valentine, who has as associates Drs. William S. Beck, James H. Follette, and E. Barton Hardin. 2. Uric acid excretion in clinical disorders associated with white blood cell abnormalities. Dr. William S. Adams, in association with Dr. William G. Figueroa, is in charge of this work. 3. Leukopheresis as a means for studying the rate of production, the rate of utilization, and the possible reserve of white blood cells in the body and other related physiological problems. The term leukopheresis is used to represent white blood cell depletion by removal from the blood, in the same sense as plasmapheresis is used to indicate removal of plasma from the blood. The investigative procedures in this field are supervised by Dr. Charles G. Craddock. Others working on this are Drs. William S. Adams and Seymour Perry.

BIOCHEMISTRY OF LEUKOCYTES

One important field of investigation by members of this laboratory in the general area of physiology of the

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white blood cells is biochemical studies. This laboratory has been interested in this field since 1948, when Valentine and myself [1] reported some observations on the histamine content of the blood. Since that time, several publications have been made dealing with segments of this general field. It has seemed to us that the leukocytes were admirably suited for such studies, since they lend themselves to sampling and study from time to time without serious inconvenience to the subject and since, as nucleated cells, they have much of the metabolic equipment of tissues more conventionally used in metabolic and biochemical studies at the cellular level, such as liver, kidney, and muscle. The myeloid leukocytes of the myelocytic and later stages of maturation store glycogen,[2] and all forms of leukocytes use glucose, produce lactic acid, and consume oxygen. Studies to date indicate the presence of all the enzymatic factors of the Embden-Myerhoff glycolytic cycle. In addition, leukocytes possess a vast enzymatic machinery whose specific uses can only be the subject of speculation in most instances. Leukocytes contain beta glucuronidase, acid and alkaline phosphatase, esterase, lipase, glyoxalase, aminopherase, adenosinetriphosphatase, and diphosphopyridine nucleotide, to name only a few of their explored activities, as well as such nonenzymatic, biologically important substances as glutathione, glucuronic acid, histamine, and glycogen. The study of leukocyte metabolism has provided information concerning (1) metabolic and biochemical differences among the same types of leukocytes at different stages of development and among different types of leukocytes and (2) the impact of disease in changing the normally observed metabolic patterns.

Glycolysis and Respiration.—Both glycolysis and respiration [3] have been found, on a per-cell basis, to be much lower in homogenates of leukocytes from persons with chronic lymphocytic and myelocytic leukemia than from normal persons. In the case of lymphocytic leukemia this difference may be explained, at least in part, by the reduced size of the lymphocyte, but this explanation cannot be used in myelocytic leukemia. It would appear that the consistent differences in glycolytic and respiratory rates in leukocytes from normal persons and persons with chronic myelocytic leukemia actually represent differences in metabolic capacities. Recent studies on isolated enzymatic components of glycolysis indicate that the lactic dehydrogenase and triose phosphate dehydrogenase content of leukemic tissue is reduced. At first there appeared to be a possible rate-limiting factor, but further studies suggest that this reduced capacity still exceeds the over-all glycolytic rate. It should be emphasized that alterations in cofactors and glycolyzable substrates will profoundly affect glycolytic and respiratory metabolic rates and ratios.

Glycogen.—Glycogen [4] is found in significant amounts only in granulocytes at the myelocytic or later maturation stages. The unit myeloid cell glycogen level is usually elevated in patients with polycythemia vera with neutrophilic leukocytosis or leukocytic immaturity, whereas it is appreciably reduced in patients with chronic myelocytic leukemia. It is of interest that it remains essentially normal in persons with uncontrolled diabetes mellitus and in those receiving cortisone.

Histamine.—Histamine [5] appears to be present only within the myeloid series of cells. Blood histamine levels as high as 250 times the upper limit of normal values have been found in persons with chronic myelocytic leukemia. Those with leukemoid reactions and neutrophilic leukocytoses do not show similar elevations of blood histamine level. It now seems probable that the basophil [6] is the chief granulocyte containing histamine and that the differences are related to differences in numbers of basophils in the cell populations analyzed.

Free Sulfhydryl (Glutathione).—Leukocytes are well supplied with sulfhydryl compounds. Our findings [7] indicate that the free sulfhydryl content of leukocytes compares favorably, on a wet weight basis, with that of many other tissues. In contrast to the findings reported by others, no increase has been observed at this laboratory to occur in leukemias or in other situations with increased leukopoietic activity.

Acid and Alkaline Phosphatase.—Normal leukocytes contain both acid and alkaline phosphatase in concentrations much above those of normal plasma. Our findings [8] have shown rather characteristic variations in alkaline phosphatase in certain clinical disorders. Specifically, the level of unit cell alkaline phosphatase is uniformly low in chronic myelocytic leukemia, high normal or high in polycythemia vera of the type with neutrophilic leukocytosis or immaturity, and high in the presence of infection, in the postoperative period, and after the administration of corticotropin (ACTH) in large doses. Very low values for both acid and alkaline phosphatase have been found in acute blastic leukemias and in chronic lymphocytic leukemia.

Beta Glucuronidase.—Substantial amounts of beta glucuronidase are present in the separated leukocytes of normal human subjects and of persons in a variety of diseased states.[9] Very low values have been found in this laboratory in acute blastic leukemia, chronic lymphocytic

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leukemia, and infectious mononucleosis, whereas normal or high values have been found in chronic myelocytic leukemia. Our findings indicate that there is a substantial amount of this substance in neutrophils and eosinophils, while it is minimal in blasts and lymphocytes.

The foregoing brief outline of some of the better established components of leukocyte metabolism is by no means complete. Leukocytes are known to contain amylase, esterase, lysozyme, proteolytic ferments, catalase, nucleotidase, and a variety of trace metals, as well as other, less well-known constituents. The table shows our findings in separated human leukocytes in leukemia and other conditions. Progress in this biochemical field has been slow, but a new set of normal standards for the white blood cells is being evolved. The exact significance of some of the variations in these substances within the white blood cells cannot be seen at this time, but one can foresee the time when study of such variations may be as valuable in certain disorders as are studies of morphological variations in the blood in various clinical diseases. Such studies should lead to a better understanding of the relationship of leukocytes to certain diseased states.

Percentage of Normal Values of Biochemical Constituents and Enzymatic Activities of Separated Human Leukocytes in Leukemia and Other Conditions*

Constituent	Blastic Leukemia	Chronic Myelocytic Leukemia	Chronic Lymphocytic Leukemia	Polycythemia Vera	Neutrophilic Leukocytes
Aerobic glycolytic rate †	....	42.2	16.4	.....	.....
Oxygen consumption †	....	30.0	27.5	.....	.....
Glucose utilization †	....	37.1	22.0	.....	.....
Lactic dehydrogenase	....	41.0	24.3	.....	.....
Triose phosphate dehydrogenase	....	58.7	19.3	.....	.....
Pyridine nucleotides	....	91.0	91.0	.....	.....
Total phosphorus	....	78.4	62.5	.....	.....
Acid-soluble phosphorus	....	70.4	45.0	.....	.....
Phospholipid phosphorus	....	66.6	32.3	.....	.....
Nucleic acid phosphorus	....	103.5	112.8	.....	.....
Phosphoprotein phosphorus	....	60.1	58.5	.....	.....
Desoxyribonucleic acid	....	97.0	105.6	.....	.....
Ribonucleic acid	....	97.7	93.8	.....	.....
Total nitrogen	....	93.7	40.3	.....	.....
Glycogen	Very low	50.5	Very low	154.7	115.4
Acid phosphatase	40.6	161.7	Low	146.1	117.3
Alkaline phosphatase	6.5	14.8	Low	308.0	476.4
Beta glucuronidase	Very low	112.8	28.7	Normal	82.3
Glucuronic acid	Very low	81.7	38.3	Normal	104.6
Free sulfhydryl	Low	107.8	56.9	100.0	94.1
Histamine	Low	High	Low	Normal	Low

* Figures represent the ratio of mean value to the normal mean. In instances in which data are insufficient to obtain satisfactory mean figures, the values are represented by a qualitative estimation.
† In a fortified homogenate system.

URIC ACID EXCRETION

Long-term observations of uric acid excretion in patients with various disorders of the blood, while on a low purine diet, have been carried out in this laboratory for some time. The conditions studied have included acute leukemia, chronic myelocytic leukemia, chronic lymphocytic leukemia, multiple myeloma, Hodgkin's disease, polycythemia vera, and myeloid metaplasia. These patients have been on the metabolism ward during the time these observations were being made. A few findings pertinent to this discussion will be mentioned.

There is a distinct relationship between the urinary uric acid excretion and the diet. The average urinary uric acid excretion of normal persons on a low purine diet was 504 mg. per 24 hours, as compared with 804 mg. per 24 hours when on a diet with a normal purine content. It would appear also that, with the reduction in urinary uric acid excretion, there was a concomitant decrease in the serum uric acid level.

Our data indicate that the total urinary uric acid excretion in patients with multiple myeloma and chronic lymphocytic leukemia is within or slightly below normal limits, whereas the quantitative excretion of uric acid is two to two and one-half times the average normal value in patients with chronic myelocytic leukemia, Hodgkin's disease, polycythemia vera, myeloid metaplasia, and acute leukemia.

In patients with leukemia, our data have shown no definite relationship between the level of leukocytes in the peripheral blood and the amount of uric acid excreted in the urine, although there has seemed to be a correlation between the severity of the leukemic process and the magnitude of the uricosuria. It would appear, therefore, that the amount of uric acid excreted may be related to the amount of neoplastic tissue undergoing destruction, either spontaneously or under the effects of therapy. In this connection it was observed that therapy of several types was accompanied by an increased uric acid excretion. X-ray therapy usually produces hyperuricuria, as has been previously reported.[10] Similar effects are produced by 4-amino-N^{10}-methylpteroyl glutamic acid (A-Methopterin), corticotropin, triethylenemelamine, and nitrogen mustard.

We have been particularly interested in the excretion of uric acid in chronic lymphocytic leukemia and have found that in most patients with this disease it is not increased. A few of the theoretical explanations of this finding may be mentioned. 1. It may be that the rate of and that its longevity is thereby increased, as Osgood [11] utilization of the lymphocyte in this disease is reduced has suggested. 2. It is possible that the degradation of

9. Follette, J. H.; Valentine, W. N., and Lawrence, J. S.: The Beta-Glucuronidase Content of Human Leukocytes in Health and Disease, J. Lab. & Clin. Med. **40**: 825 1952.

nucleoprotein results in end-products other than uric acid. 3. Uric acid may be destroyed or reincorporated in some unknown metabolic pathway. In the last analysis, an explanation of this absence of increased excretion of uric acid in chronic lymphocytic leukemia is not at hand.

LEUKOPHERESIS

For many years it has seemed to us most important to have accurate data relating to the reserve and the rate of utilization of the white blood cells. Factual data of this sort on the red blood cell have been known for a long time. Thus, the length of life of the red blood cell has been shown by various methods to be about 120 days in the average normal person.[12] The rate of regeneration of the red blood cell is also well known. The blood platelet has been similarly, though less thoroughly, studied. The rate of utilization of the platelet in the cat was determined by Lawrence and Valentine in 1947.[13] Review of the available literature at that time showed that there was very little work on which to base any conclusive estimate as to the life span of the platelet. Following the report of Lawrence and Valentine it has been amply shown that the time survival of platelets in man is about the same as that found by these authors in irradiated thrombopenic cats, namely, two to five days.[14] Studies in this connection with reference to the white blood cells have yielded much less definitive and conclusive data. The length of life of the white blood cell has been estimated by various methods, with results that are by no means consistent. A review of the various estimates of the life span and the rate of utilization of the white blood cell was made in 1945,[15] at which time they ranged from one year [16] to a few hours.[17] The data of Lawrence and others in 1945 pointed to a rate of utilization in the cat of about 12 to 18 hours.[15] Various estimates of the survival of leukocytes were reported by several investigators at the Conference on the Preservation of the Formed Elements and of the Proteins of the Blood at the Harvard Medical School in January, 1949.[18] One of the most recent methods used in this problem has been the use of the rate of incorporation of radioactive phosphorus (P^{32}) into desoxyribosenucleic acid. Osgood and associates,[19] by the use of this method, have presented data that they have interpreted as indicative of a life span of three days or less for cells of the granulocytic series in patients with granulocytic leukemia. On the other hand, their data pointed to a life span of 30 days for the lymphocyte in patients with chronic lymphocytic leukemia. Kline and Cliffton,[20] using similar methods, estimated the life span of the leukocytes to be 13.2 days. Bierman and co-authors [21] have used cross circulation in man much as we did in the cat. Their observations showed that white blood cells given in this way left the circulating blood at a rapid rate (28,000 to 34,000 per cubic millimeter per day in one experiment).

Materials and Methods of Study.—Our most recent approach to the problem of leukopoiesis has been by means of leukopheresis. Details of the procedure will be published elsewhere. In brief, mongrel male dogs were used. Pentobarbital anesthesia was induced, after which cannulation of one femoral artery and one femoral vein was done. Blood was removed in aliquots of 40 to 50 cc. and collected in plastic centrifuge tubes containing 0.3 ml. of 10% ethylenediaminetetraacetate disodium (Sequestrene). Most of the white blood cells and the platelets were removed by centrifugation and suction. The red blood cells and plasma were then mixed and readministered to the animal. Due to the time involved in carrying out this procedure, there was some deficit of blood in the animal, but shock was not encountered and was prevented by the administration of blood previously collected from the same dog or Ringer's solution, or both. After the first specimen of blood had had its white blood cells and platelets removed and was ready for reintroduction into the animal, there was no further deficit of blood, as the same amount of blood depleted of white blood cells and platelets was given by vein as was obtained by artery thereafter. The technique has been developed to the point that leukopheresis can be carried out at a very rapid rate, one or more blood volumes being leukopheresed during the period of one hour. Each animal received 600,000 units of procaine penicillin and 250 mg. of streptomycin intramuscularly at the beginning of the experiment. Replacement of calcium, if indicated, was controlled by electrocardiographic changes. Blood volume determination was made by the Evans blue dye method. White blood cell counts, platelet counts, hematocrit determinations, and differential counts on smears of the blood were made on all specimens of blood. Bone marrow studies were made at appropriate intervals. Some animals were irradiated. These were given whole body irradiation with the medial lethal dose. With the technique used, the amount of irradiation was 200 r given over a 15 to 20 minute period as delivered from two heads, one placed above and one below the animal. This amount of irradiation delivered in this way has been found to approximate 300 to 350 r as ordinarily given. All animals receiving this dosage showed severe bone

10. Bloch B.: Beitrage zur Kenntnis des Purinstoffwechsels beim Menschen, Deutsches, Arch. klin Med. **83**: 499, 1905. Fine, M. S., and Chace, A. F.: Uric Acid Concentration of the Blood as Influenced by Atophan and Radium Emanation, J. Pharmacol. & Exper. Therap. **6**: 219, 1914. Gudzent, F.: Ueber Dosierung und Methodik der Anwendung radioaktiver Stoffe bei Inneren Krankheiten und die erzielten Heilwirkungen, Berl. klin. Wchnschr. **50**: 1597, 1913. Kerb, J. A., und Lazarus, P.: Zur Frage des Abbaues von Mononatriumurat unter dem Einfluss von Radiumemanation bzw. Radium D, Biochem. Ztschr. **42**: 82, 1912. von Knaffl-Lenz, E., and Wiechowski, W.: Über die Wirkung von Radiumemanation auf Mononatriumurat, Ztschr. physiol. Chem. **77**: 303, 1912. Okaue, S.: Über den Einfluss der Röntgenstrahlen auf den Harnsaurestoffwechsel, Folia pharmacol. japon. (Brev.) **19**: 259, 1934, cited in Kongresszentralbl. inn. Med. **80**: 523, 1935. Starkenstein, E.: Beitrage zur Physiologie und Pharmakologie des Purinhaushaltes: Die Beeinflussung des Purinhaushaltes durch Atophan, Calciumsalze, und Radiumemanation, Biochem. Ztschr. **106**: 139, 1920.

11. Osgood, E. E., and others: Growth of Human Leukemic Leukocytes in Vitro and in Vivo as Measured by Uptake of P_{32} in Desoxyribosenucleic Acid, Science **114**: 95, 1951.

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13. Lawrence, J. S., and Valentine, W. N.: The Blood Platelets: The Rate of Their Utilization in the Cat, Blood **2**: 40, 1947.

14. Hirsch, E. O., and Gardner, F. H.: Life Span of Transfused Human Blood Platelets, J. Clin. Invest. **30**: 649, 1951. Stefanini, M.; Chatterjea, J. B., and Dameshek, W.: Rate of Platelet Survival in Thrombocytopenia, ibid. **30**: 676, 1951.

marrow damage, as would be expected with a heavy dose of irradiation. Seventeen animals have been studied sufficiently to justify the use of data.

Figures 1, 2, and 3 show findings in typical experiments. Figure 1 illustrates (1) a rather precipitous drop in the number of white blood cells in the peripheral blood, (2) stabilization of the white blood cell level at a leukopenic level while leukopheresis was in progress, (3) a lag period following the cessation of leukopheresis, (4) marked increase in the number of white blood cells following the lag period, (5) "overshooting" of the white blood cell level (330%), and (6) failure of epinephrine to cause an increase in the white blood cell level when given during the leukopenic phase of the exchange. Figure 2 shows the failure to produce a marked reduction in the white blood cell level over a period of 14 hours when the rate at which the blood was cleared of leukocytes was less than one blood volume per hour, whereas marked leukopenia was readily induced when the rate

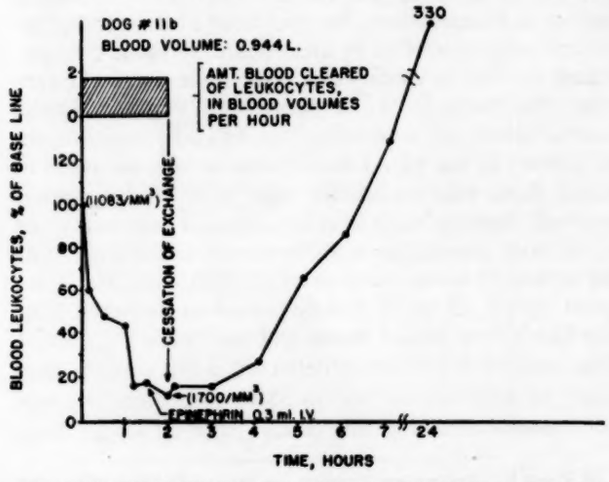

Fig. 1.—Change in leukocyte level incident to leukopheresis in a normal dog. Note the time that leukopenia persisted after termination of the procedure and the failure of epinephrine to elevate the leukocyte level.

of depletion of white blood cells was increased. It is worthy of comment that the length of the lag period was not changed by this long period of leukopheresis. Figure 3 reveals the average findings in nine normal dogs.

Rate of Entry of Leukocytes into Circulation.—The number of blood volumes leukopheresed per hour in order to accomplish maximum leukopenia has been found to average 1.9 blood volumes per hour. In terms of liters, the clearance was 0.69 to 2.03 liters per hour, with an average of 1.49 liters per hour. In broad terms, the circulating blood volume must be cleared of leukocytes in a normal dog within somewhat less than an hour to exceed the rate of entry of these cells into the circulating blood. If the average leukocyte level of the normal dog is assumed to be 10,800 cells per cubic millimeter with 75% granulocytes, and the average blood volume is

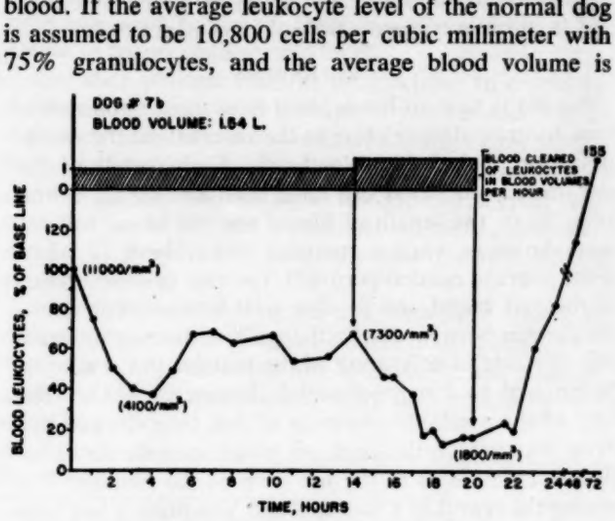

Fig. 2.—Prolonged leukopheresis in a normal dog without effecting a marked leukopenia until the rate of removal of leukocytes was increased.

taken as one liter, the rate of entry of myeloid cells into the peripheral blood at the onset of the exchange must have been less than 0.8×10^{10} cells per hour, since marked leukopenia would not have resulted otherwise. In these calculations, it has been assumed that the rate of entry of myeloid cells remains fairly constant over the period during which the exchange is taking place.

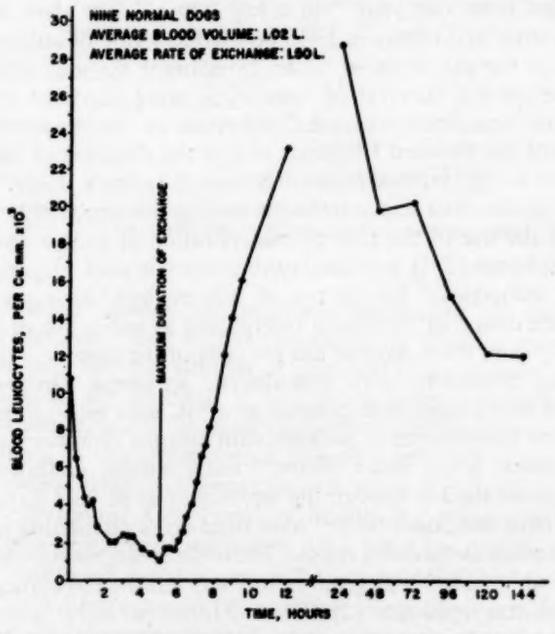
NINE NORMAL DOGS
AVERAGE BLOOD VOLUME: 1.02 L.
AVERAGE RATE OF EXCHANGE: 1.80 L.
MAXIMUM DURATION OF EXCHANGE
BLOOD LEUKOCYTES, PER Cu. mm. x10³
TIME, HOURS

Fig. 3.—Average leukocyte counts on nine normal dogs. The rate and duration of leukopheresis differed for each animal. The arrow denotes the longest period of exchange in this group.

The bulk of our evidence, however, indicates that this assumption is not correct. Some attempts have been made to quantitate the rate of entry by the rate of removal. In one typical instance, reducing the clearance rate by 50% failed to produce leukopenia of any appreciable extent, whereas a further increase in the rate again

15. Lawrence, J. S.; Ervin, D. M., and Wetrich, R. M.: Life Cycle of White Blood Cells: The Rate of Disappearance of Leukocytes from the Peripheral Blood of Leukopenic Cats, Am. J. Physiol. **144**: 284, 1945.

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17. Minot, G. R., and Isaacs, R.: Transfusion of Lymphocytes: Their Rapid Disappearance from the Peripheral Circulation of Man, J. A. M.A. **84**: 1713 (June 6) 1925.

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19. Osgood, E. E., and others: The Relative Rates of Formation of New Leukocytes in Patients with Acute and Chronic Leukemias: Measured by the Uptake of Radioactive Phosphorus in the Isolated Desoxyribosenucleic Acid, Cancer **5**: 331, 1952.

20. Kline, D. L., and Cliffton, E. E.: Lifespan of Leucocytes in Man, J. Appl. Physiol. **5**: 79, 1952.

21. Bierman, H. R.; Byron, L., and Lanman, J. T.: Cross-Circulation Studies in Man, Bull. Univ. Calif. M. Center **1**: 89, 1949.

produced leukopenia. In this experiment, it would appear that clearance of the cells from the blood at the rate of 50% of the cells per hour did not produce leukopenia over a two and one-half hour period. This would mean removal of 0.6×10^{10} cells in this particular animal per hour. From the slopes of the curves of recovery, it appears that the recovery rate after the initial depletion was about 0.25×10^{10} cells entering the circulation per hour. The second recovery curve was considerably faster, about 1.7×10^{10} cells per hour. This type of accelerated

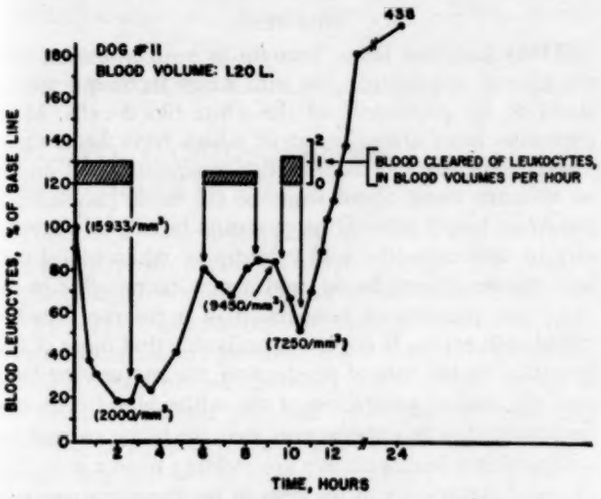

Fig. 4.—The effect of reinstituting leukopheresis in a normal dog. The second period of leukopheresis was performed at one half the rate of the first. No leukopenia ensued. The third leukopheresis was performed at one and a half times the initial rate and caused depression of leukocytes. Note the absence of any delay in the leukocytosis after the third leukopheresis and the accelerated rate of entry of cells into the circulation.

recovery after repeated exchange was observed several times. It would seem, therefore, that with repeated depletion the rate of entry of cells into the circulation accelerates. Hence, the assumption that the rate of entry of cells into the circulation remains constant in the presence of repeated leukopenia cannot be made. In several instances, epinephrine was given intravenously at the time of maximal leukopenia. There was no significant change in the white blood cell level as a result of this.

The rate of return of leukocytes in the peripheral blood of normal animals after initial production of maximal leukopenia was observed closely. Ten animals were available for such studies. The level of white blood cells returned to the normal value in about four and one-half hours, the actual level at this time varying between 90 and 132% of normal. It may be noteworthy that there was a lag phase of 60 to 90 minutes before the rapid rise in the leukocyte level began. In every normal animal a level of 5,000 white blood cells per cubic millimeter had been reached in two to three hours. The curve after the initial lag period is essentially a straight line for six to seven hours after the end of the first postexchange hour. It is of significance that in this normal group of animals the time of onset and the rate of rise of the leukocyte level remained the same regardless of how long the leukopenia, once induced, had been maintained by continuous exchange. The leukocyte level invariably overshot the normal level within 24 hours, values of 300% or more of normal being reached.

Cell Studies.—Differential white blood cell counts in the normal animals showed a mild to moderate shift to the left, beginning during the early part of the recovery phase. None showed immaturity of the cell population during the actual exchange period. For the most part, the shift to the left at the beginning of recovery involved an increase in stab forms with only a scattering of more immature forms. However, at 24 hours considerable numbers of juvenile forms and myelocytes were present. In most of the animals, the lymphocytes almost disappeared. Their numbers declined sharply during the period of exchange and remained low throughout the recovery period. Bone marrow studies have been done serially on six animals; however, these studies are by no means complete. The findings reveal a significant decrease in the relative numbers of mature myeloid forms at the time of maximal leukopenia, whereas there is a mild to moderate myeloid preponderance with an increased percentage of myelocytes, promyelocytes, and blast forms 24 hours after the exchange.

Results in Irradiated Animals.—It has seemed particularly pertinent to study the response of irradiated animals to these procedures prior to the time when maximal irradiation leukopenia developed in them. Accordingly,

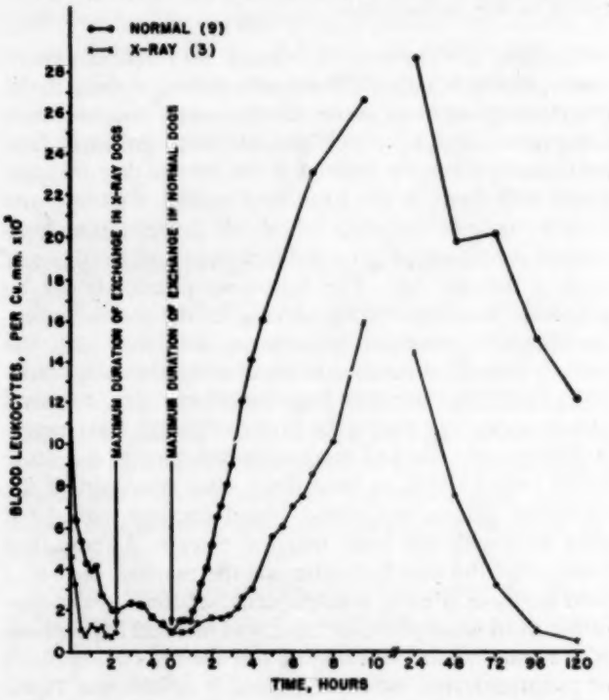
NORMAL (9)
X-RAY (3)
MAXIMUM DURATION OF EXCHANGE IN X-RAY DOGS
MAXIMUM DURATION OF EXCHANGE IN NORMAL DOGS
BLOOD LEUKOCYTES, PER Cu.mm. x10³
TIME, HOURS

Fig. 5.—Comparative response of three irradiated dogs (exposed to LD_{50} at intervals of 18, 36, and 42 hours, respectively, prior to leukopheresis) and nine normal dogs. The point of cessation of exchange has been approximated for the two groups in order to make the recovery phase more readily comparable.

a few animals have been observed at varying intervals after irradiation (1, 18, 36, and 42 hours). In general, it may be said that (1) maximal leukopenia developed more promptly than in normal animals, (2) the lag period following exchange was longer (three hours), (3) the rate of entrance of cells into the peripheral blood once recovery had begun was the same percentagewise but much less numerically than in the normal animals, and (4) the total level of leukocytes surpassed the preex-

change level by as much as 300% at the end of 24 hours after leukopheresis. In all of these animals, complete aplasia of the marrow was found on examination after death (survivors were killed eight days after irradiation). Figure 5 illustrates these results in three irradiated animals. Bone marrow of none of these was aplastic prior to leukopheresis, the only marked change being a relative increase in mature myeloid forms. It showed a marked decrease in cellularity 24 hours after exchange.

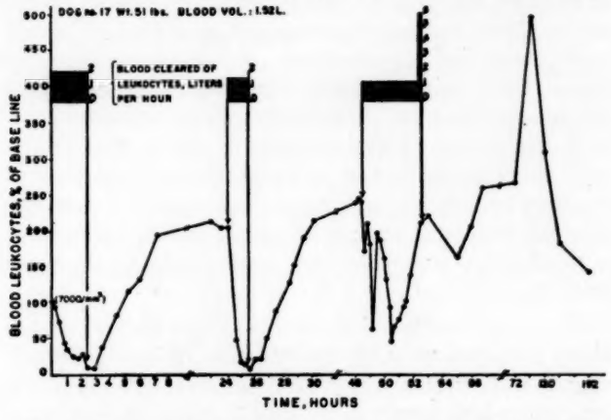

Fig. 6.—The response of the leukocyte count in a normal dog to leukopheresis on three successive days.

Multiple Leukophereses.—Some very recent experiments, in which leukopheresis sufficient to produce maximal leukopenia was done in the same dog on three consecutive days, have yielded some very significant data, particularly when the findings in the normal dog are compared with those in the irradiated animal. Figure 6 and 7 show some of the white blood cell changes in animals treated in this way. Figure 6 illustrates the data obtained from a normal dog. The following points should be noted: 1. The slope of the curve after the second leukopheresis was somewhat more steep than that after the first. 2. Despite about four hours of leukopheresis, reaching a rate of 6 liters per hour for 10 minutes, the level of leukocytes rose during the period of the third exchange. 3. There was a marked increase in the level of the white blood cells (500% of base line) after cessation of the exchange. These peripheral blood findings correlated very well with the bone marrow picture. Twenty-four hours after the first leukopheresis the marrow showed a mild increase in early myeloid cells, whereas at the time of the third leukopheresis there was marked hyperplasia of the marrow, the vast majority of the cells being blasts or promyelocytes, or both. Figure 7 reveals the blood findings in an irradiated animal on which multiple leukophereses were performed. Leukocytosis followed the first and second leukophereses, but the slope of the second recovery curve was much lower than that of the first. After the third leukopheresis, the white blood cells gradually disappeared from the blood. The bone marrow of this animal at the time of the first leukopheresis (one hour after irradiation) appeared morphologically normal. At the time of the second leukopheresis, it showed relatively few myelocytes and many cells in later stages of development but no early or parent cells. Twenty-four hours later (third leukopheresis) the only white blood cells present in the marrow were late forms—stabs and segmented types. There were many of these. These results have been repeated in other experiments. One possible explanation of the findings in the irradiated animal is that the early or parent cells were destroyed by irradiation. As a result, the animal used what cells it had left, and eventually all of these were exhausted or used, all of the cells capable of division having progressed to the adult forms. If this is correct, it should be possible to calculate accurately the potential reserve of white blood cells in the marrow by the use of such animals. Our findings at this time indicate a very large potential reserve.

COMMENT

These data are being brought to your attention with the idea of acquainting you with a new technique for the study of the physiology of the white blood cells. Many problems have arisen, most of which have been unanswered. However, I believe this procedure will enable us to learn more about some of the basic problems of the white blood cells. Thus, it should be possible eventually to determine the rate of entry of white blood cells into the peripheral blood, and it may be possible to answer the question of how much of a reserve of white blood cells exists. It is even conceivable that more definitive data on the rate of production, the maturation time, and the rate of utilization of the white blood cells may be obtained. The experiments that are being carried out with multiple leukopheresis are yielding results indicative of rapid maturation of the cells in the bone marrow with marked myeloid hyperplasia of the marrow after the third leukopheresis in normal animals, as contrasted with a depleted marrow having only cells late in maturation in irradiated animals treated similarly. These observations also confirm previous suspicions that the parent cells are the ones primarily affected by irradiation, the cells later

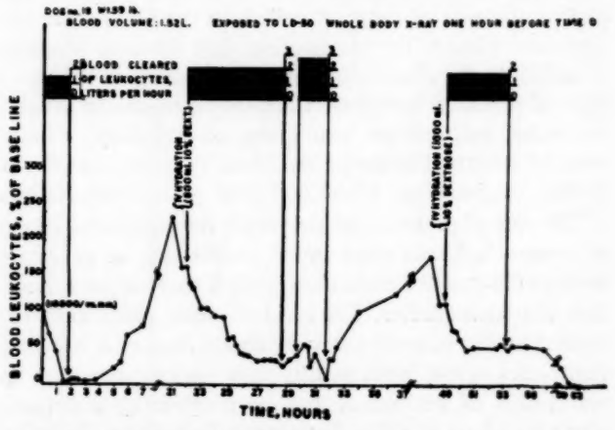

Fig. 7.—The response of the leukocyte count in a dog exposed to LD_{50} whole body x-ray one hour prior to experiment. During the leukopheresis 18×10^{10} cells were removed.

in maturation proceeding to the normal development. It is planned to use this technique in the study of factors concerned in the control of white blood cell growth in the marrow and the release of such cells into the peripheral blood. Biochemical and leukopheretic techniques may aid materially in our understanding of the white blood cells in normal and diseased states. Such studies should provide much information about these cells that cannot be gotten by purely morphological studies.

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STELLATE GANGLION BLOCK AND APOPLEXY

There is always a tendency in emergency treatment to use any means that might possibly benefit the patient. It often requires courage to withhold such a treatment for the purpose of accumulating enough controls to make a critical evaluation possible. This inevitably gives rise to controversy. Such a controversy exists with regard to the value of stellate ganglion block in the emergency treatment of apoplexy. De Takats [1] favors this procedure on the basis that (1) clinical reports show early improvement in the neurological signs and symptoms in patients so treated; (2) this treatment decreases cerebral vascular resistance; (3) in 60% of the cases of cerebral infarction there was no postmortem evidence of occlusion of the cerebral vessels by embolism, thrombosis, or arteriosclerosis, and in only a few was there shock or heart failure, thus pointing to vasoconstriction as the cause of ischemia; (4) it produces increased vascularity of the brain; and (5) cervical sympathetic stimulation in animals produces dilatation of intracranial vessels on the side opposite the excitation.

De Takats also lists the arguments against this procedure: 1. The vasomotor control of the cerebral vessels is weak. 2. The cerebral vessels do not engage in the regulation of body heat, and the blood flow to the brain is maintained as evenly as possible. 3. The vessels of the pia have been seen to contract in experimental embolism, and this vasoconstriction could be abolished by cervical sympathetic block. 4. Experimental section of the cervical sympathetic trunk results in increased blood flow in the extracranial regions but not the intracranial region. 5. Bilateral stellate ganglion block does not significantly affect cerebral blood flow or cerebral vascular resistance in normal or hypertensive persons. 6. The vasodilator effects of increased carbon dioxide or decreased oxygen concentrations are definite, and general vasodilators such as histamine produce a measurable increase in cerebral circulation, in contrast with the effect of sympathetic block. 7. Some clinical reports deny any improvement from such treatment in patients with apoplexy.

Millikan and his co-workers [2] call attention to the fact that although marked improvement may occur spontaneously after an acute focal lesion of the brain the advocates of stellate ganglion block neither take this into account nor present a controlled series. Their own controlled series, although admittedly too small to form a basis for conclusive results, may later be combined with similar series from these or other authors and help resolve this controversy. They observed no significant difference in the results of treatment with and without cervical sympathetic nerve block. Ruben and Mayer [3] in a small uncontrolled series of patients treated with block noted improvement in 60%. Admitting that their results were inconclusive, they advocated using this procedure as an adjunct to good nursing care until a better treatment is found. They might have added "or until the value or lack of value of this measure has been firmly established."

De Takats states that failure to obtain good results from stellate ganglion block may be due to spreading intracerebral hemorrhage and edema, intraventricular hemorrhage, applying the block too late, severe vascular sclerosis, shock-like state and loss of consciousness, and insufficiency of the circle of Willis. He believes that if the patients who might be expected to benefit from stellate ganglion block could be selected with greater certainty the failure rate would be reduced, but some of these factors cannot be determined, and in an emergency elaborate and time-consuming examinations cannot be made. Because the procedure is relatively simple and because it produces no harmful complications, there would appear to be no serious objection to its continued use, but the need for an objective approach to the problem is great.

CANDIDATES FOR A. M. A. AWARD

With the annual A. M. A. convention in Atlantic City coming up in June, members of the Association are encouraged to submit as soon as possible the names of candidates for the Distinguished Service award. Councils or trustees within the various state societies are urged to nominate candidates. The name of the candidate and a biographical sketch outlining his meritorious services should be mailed to the Secretary's office at A. M. A. headquarters.

During the Miami meeting last December, the Board of Trustees decided that if a candidate is not selected by the House of Delegates after two years his name will be dropped from the list and not carried over from year to year. The recipient of the award, which is granted for outstanding contributions to medicine and to humanity, is chosen in an election by the House of Delegates at the opening session. Formal presentation of the award, which includes a gold medal and a citation, will be made on Tuesday night, June 7, at the inaugural ceremony for the new A. M. A. President.

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THE BURNETT OR MILK-ALKALI SYNDROME

Burnett and his co-workers [1] described in 1949 a syndrome that has many features in common with primary hyperparathyroidism with secondary kidney damage. This particular syndrome, however, has an entirely different etiology. The characteristic features they had observed in their series of six patients consisted of a history of prolonged and excessive intake of milk and of absorbable alkalies. The other features were hypercalcemia without hypercalciuria or hyperphosphatemia; normal serum alkali phosphatase level; marked renal insufficiency with azotemia; mild alkalosis; calcinosis manifested especially by an ocular lesion resembling band keratitis; and what was most important, improvement in the clinical state with an intake low in milk and absorbable alkali.

The most striking physical finding in their patients and the only one common to all six was found in the eyes. These lesions were believed to be associated with hypercalcemia. One of these is "band keratopathy." The other type of lesion consisted of small glass-like particles in the conjunctiva of the palpebral fissure area. Biopsy of this type of lesion in one of the patients in the series reported on by Walsh and Howard [2] showed an amorphous material, presumably a calcium salt beneath the conjunctiva, and keratopathy was present in all of their patients; in two the conjunctival lesions were also present.

Pruritus was a prominent complaint in four of the six patients. There was definite hypercalcemia in five, the serum calcium level varying between 12.0 and 14.5 mg. per 100 cc. The results of various renal function tests all indicated advanced renal disease. Ability to concentrate the urine was uniformly absent. Although primary hyperparathyroidism was suspected in all of the patients, the syndrome differed from it by the following features: lack of hypophosphatemia in the presence of hypercalcemia, lack of hypercalciuria, lowering of the serum calcium with a low calcium intake and absence of skeletal demineralization, and elevation of serum alkaline phosphatase.

The possibility that ulcer regimens in which milk and absorbable alkali are used may adversely affect kidney function has been suggested repeatedly. It is also well known that acute alkalosis may cause a marked diminution in renal function and that a subsequent striking improvement may occur after correction of the alkalosis. These authors stress, however, that definite proof that alkalosis can cause permanent renal damage is lacking. In their own series the patients had no episodes of acute alkalosis with accompanying azotemia. They were all found to be suffering from chronic renal failure.

Although primary hyperparathyroidism could not be excluded in all of their patients, the evidence presented suggests that the abnormalities observed in the calcium and phosphorus metabolism were a result of excessive intake of milk and alkalies followed by kidney damage and a tendency to fixation in urinary calcium excretion, hypercalcemia, and calcinosis. The improvement that resulted from a low intake of milk and absorbable alkalies supports this sequence of events.

Miller and Freeman [3] reported on a patient with a duodenal ulcer and a prolonged history of high intake of milk and absorbable alkalies. There was deposition of calcium in his eyes and in the lumbar region. Hypercalcemia, normal serum phosphorus and serum alkaline phosphatase levels, mild alkalosis, and a severe degree of renal impairment were found. The ulcer was successfully treated by a partial gastric resection. There was improvement in renal function. The serum calcium level returned to normal; the calcium deposition in the eyes and in the lumbar region, however, were not altered. Dworetzky [4] observed a case of metastatic calcinosis secondary to prolonged high intake of milk and alkali because of chronic duodenal ulcer and striking disappearance of the calcinosis when the excessive intake of milk was eliminated and aluminum hydroxide gel was substituted for the absorbable alkali. McQueen's [5] patient had been drinking about a gallon of milk a day. He also took aluminum hydroxide gel and alkaline powder alternating each for a month at a time. He developed painful swellings in the wrist and dorsum of the left hand and in the elbow. His serum calcium level and carbon dioxide combining power were high while serum phosphorus and serum alkaline phosphatase levels were normal. When milk and other calcium-containing foods were removed from his diet, the symptoms and most of the calcium deposits disappeared. Wermer and co-workers [6] were also able to report regression of ocular and subcutaneous lesions following dietary restriction of calcium in a patient with metastatic calcification following prolonged high intake of milk and alkali.

The case reported by Carpenter and Pautler [7] showed most of the features of the Burnett syndrome; however, postmortem revealed the presence of a parathyroid adenoma. They therefore concluded that the Burnett syndrome is probably after all a primary hyperparathyroidism associated with an excessive intake of milk and absorbable alkali.

Kyle [8] stresses the difficulty in differentiating primary hyperparathyroidism from the milk-alkali syndrome. He had observed two patients who showed all of the criteria for the diagnosis of dietary hypercalcemia. One of these patients, however, was shown to have a parathyroid adenoma. The presence of the milk-alkali syndrome was strongly suggested by the combination of azotemia and alkalosis. Band keratopathy and pruritus, emphasized by Burnett as characteristic of his syndrome, can occur in other hypercalcemic disorders, but appeared to be particularly frequent in patients who ingest large amounts of milk and alkali.

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ORGANIZATION SECTION

FEDERAL MEDICAL LEGISLATION

Sixth Installment, First Session, 84th Congress

Narcotic Traffic

Congressman Thornberry (D., Texas), in H. R. 87, would authorize the appointment by the Speaker of the House of a committee of five members of the House that would be "authorized and directed to conduct a full and complete investigation and study of the problems involved in controlling illicit traffic in narcotic drugs, and marihuana, and combating the increasing narcotic addiction in the United States." Hearings could be held inside and outside of the United States. Subpoenas would be authorized and the committee directed to report to the House "during the present Congress the results of its investigation and study, together with such recommendations as it deems advisable." This bill was referred to the Committee on Rules.

Reinsurance

Congressman Wolverton (R., N. J.), in H. R. 2533, has introduced a measure essentially similar to H. R. 8356 in the previous Congress that was favorably reported to the House by the Interstate and Foreign Commerce Committee and was recommitted by floor action. He would establish a reinsurance program with a 25 million dollar authorization advanced for working capital. Private insurance companies, voluntary nonprofit health associations, and prepayment health insurance plans could purchase reinsurance for a premium. This bill was referred to the Committee on Interstate and Foreign Commerce.

Disability Insurance

Congressman Van Zandt (R., Pa.), in H. R. 2212, would grant disability benefits to the disabled at the time of disability instead of waiting until the retirement age of 65 years. Congressman Hayworth (D., Mich.) has introduced H. R. 2844, a similar measure. Both measures were referred to the Committee on Ways and Means. Congressman King (D., Mich.) has introduced a similar measure, H. R. 2608, giving disability payments to the disabled after six months disability. An additional provision is that the $1,200 annual work income limit may be waived for disabled persons if their work helps to rehabilitate them. The Secretary of Health, Education, and Welfare could discontinue disability benefits if the individual would refuse to submit to examination or reexamination, would refuse to accept state rehabilitation services under the Vocational Rehabilitation Act, or if the person were no longer disabled. In determining disability, the Secretary could seek the cooperation of or enter into voluntary working agreements with federal and state agencies, private medical and hospital groups, or other organizations. If disability examinations were made by private physicians, the Secretary would pay the fee. To insure prompt and regular payments of benefits, the Secretary could contract with a state agency without first knowing that the agency would be able to make disability determinations rapidly and efficiently. If determinations were not made promptly, the Secretary would terminate the agreement with the state agency. This bill was referred to the Committee on Ways and Means.

Hospitalization for Aged

Congressman Dingell (D., Mich.) has introduced a measure, H. R. 2384, that would provide federally paid hospitalization for persons 65 years of age and over who are covered by Old-Age and Survivors Insurance. There would be a 60-day annual limit on hospitalization. Persons with tuberculosis and mental disease would not be eligible, nor would domiciliary care be provided. This bill is identical with H. R. 638 introduced by Congressman Celler (D., N. Y.) and previously reported in more detail. It is also identical with measures introduced in the last two Congresses. This measure was referred to the Committee on Ways and Means.

Prepared by the Washington Office of the American Medical Association.

Federal Scholarships and Insurance of Student Loans

Congressman Thompson (D., N. J.) would, in H. R. 2211, provide for federal grants to states starting at 32 million dollars and reaching 128 million dollars in four years for scholarships in all fields of higher education. The program would be administered by the U. S. Commissioner of Education, who would issue regulations on the amount of stipends and selection of the students. Able and needy students, including those in premedical courses, would be eligible for four-year scholarships up to $800 per year. Subsequently for attending professional schools, including medical schools, students would be eligible for loans up to $600 or a maximum of $2,400, to be insured by the federal government. Similar bills have been introduced in previous Congresses. This measure was referred to the Committee on Education and Labor.

Commission on Nursing Services

Congresswoman Frances P. Bolton (R., Ohio), in H. J. Res. 171, would establish a 12 member commission on nursing services to aid the "nursing profession in its efforts to achieve greater efficiency and improved nursing services." The commission would be appointed by the President of the United States, the President of the Senate, and the Speaker of the House, who would each appoint four members, one-half in government and Congress and one-half in private life. The nursing and medical professions would be represented on the commission, which would gather data for all types of nursing services—professional and practical nursing and nursing aides—and would make interim reports to Congress and a final report within two years, after which the commission would expire. This measure was referred to the Committee on Interstate and Foreign Commerce.

Tax Deferment for Self-Employed

Congressman Gwinn (R., N. Y.), in H. R. 2592; Congressman Miller (R., N. Y.), in H. R. 2633; Congressman Gamble (R., N. Y.), in H. R. 3113; and Congressman Coudert (R., N. Y.), in H. R. 3574, have introduced identical measures with that of Congressman Ray (R., N. Y.), in H. R. 2092, previously reported. These bills would "encourage the establishment of voluntary pension plans by individuals." For the purpose of income tax they would allow as deduction from the gross income, "amounts paid into a restricted retirement annuity contract." This amount for a taxable year "shall not exceed the lesser of—

"(A) 2½ percent of the taxpayer's earned adjusted gross income from covered sources plus 5 percent of his earned adjusted gross income from all other sources, or

"(B) $1,000 in the case of a taxable year beginning after December 31, 1955, and ending before July 1, 1957, $2,000 in the case of a taxable year ending after June 30, 1957, and before July 1, 1958; and $3,000 in the case of a taxable year ending after June 30, 1958."

"Covered" income for the purposes of the bill means income from a corporation, association, or governmental unit that contributes to a recognized pension or retirement plan. The self-employed would be allowed 5% deduction. There is a special arrangement for those who become 50 years of age before Jan. 1, 1956, to build up their retirement at a faster rate. Provision is made for carrying over a limited amount of unused exclusions. The above bills were referred to the Committee on Ways and Means.

MISTAKEN IDENTIFICATION

The editors of *This Week* magazine, with whom members of the American Medical Association have cooperated in the current series of articles on preventive medicine, have asked THE JOURNAL to call the attention of its readers to an error in *This Week* (issue of April 3, 1955), in which Dr. Charles S. Cameron was identified as Medical and Scientific Director of the American Medical Association. Dr. Cameron is Medical and Scientific Director of the American Cancer Society. A correction will be published in *This Week* at the earliest opportunity.

MEDICAL NEWS

ALABAMA

John A. Andrew Clinical Society.—The 43rd annual clinic and the 37th annual meeting of the John A. Andrew Clinical Society will take place at Tuskegee Institute, April 3-8 under the presidency of Dr. Richard M. Haskins, Columbus, Ga. Speaking at the opening meeting in the institute chapel Sunday evening, 7 p. m., will be Dr. W. Clark Bailey, Harlan, Ky., Vice-President of the American Medical Association, who will talk on the program of the association. The meeting this year will honor Dr. Henry C. Bryant of Birmingham, one of the originators of the John A. Andrew Clinic in 1912 and the John A. Andrew Clinical Society in 1918. A citation will be presented to Dr. Bryant at the annual banquet, at which the speaker will be J. Ernest Wilkins, assistant secretary of labor. Dr. Robert Elman, professor of surgery, Washington University School of Medicine, St. Louis, will deliver the first oration on surgery in memory of the late Dr. Charles R. Drew. Dr. Drew, who was formerly affiliated with Howard University Medical School and Freedmen's Hospital, where he developed postgraduate training and residencies in the various specialties for Negro physicians, was one of the original investigators in working out the problems connected with the preservation of blood plasma to be shipped to England for use in the early days of World War II. Dr. Kenneth B. Babcock, director, Joint Commission on Hospital Accreditation, will discuss the step-by-step processes required to gain approval and the standards that must be maintained for accreditation. President L. H. Foster of Tuskegee Institute extends a cordial welcome to physicians and their families to visit the institution.

CALIFORNIA

Industrial Uses of Atomic Energy.—"Atomic Energy—the New Frontier" will be the theme of the first West Coast conference on applied industrial uses of atomic energy April 4-5 at the Mark Hopkins Hotel, San Francisco, which will be given under the joint sponsorship of the Stanford Research Institute and the Atomic Industrial Forum, New York. Among the topics to be discussed will be recent progress in the development of nuclear power plants; the potential uses of nuclear reactors for industrial research and the production of process heat and radiation; and the applications of atomic energy in the food industry, including cold sterilization and the eradication of insects.

Course on Surgical Planing.—The University of Southern California medical extension division and the department of dermatology will present a course (862) on surgical planing, consisting of five sessions of two hours each devoted to lectures and discussion covering history, indications, contraindications, histology, equipment, and results of surgical planing. Equal time at each session will be devoted to didactic presentation and informal discussion. In addition the class will be scheduled in groups of about 10 students each for a sixth session of manikin practice and demonstration of planing on patients. The first lecture-seminar will be given April 8, 7:30-9:30 p. m., preceded by manikin practice and demonstrations, 12:30-1:30 p. m. The lecture-seminar will be presented in the Medical Research Building, 2025 Zonal Ave. (across from the Los Angeles County Hospital) and the demonstrations in Los Angeles County Hospital. Tuition ($25) should be sent to Medical Extension Education, University of Southern California School of Medicine, 2025 Zonal Ave., Los Angeles 33. Registration is limited to graduates of grade A medical schools who have completed an approved internship. Because of space limitation, the course will be limited to 50 registrants.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

DISTRICT OF COLUMBIA

Hahnemann Bicentennial.—The bicentennial anniversary of the birth of Dr. S. C. F. Hahnemann will be celebrated in Washington, D. C., April 10-15, as a feature of the 111th annual convention of the American Institute of Homeopathy. Allied medical groups invited to participate include the International Hahnemannian Association, the Southern Homeopathic Medical Association, and the Pan American Homeopathic Medical Congress. Distinguished guests include Sir John Weir of London, physician to the royal family of England; Dr. Pierre Schmidt of Geneva, Switzerland; Dr. Amaro Azevedo of Rio de Janeiro, Brazil; and Dr. Riccardo Galeazzi-Lisi, physician to Pope Pius XII in Rome. On Tuesday Dr. Weir will present "Reflection of 45 Years' Practice of Homeopathy." Dr. Schmidt will have as his topic on Thursday "Homeopathy in the Atomic Age" and on Friday, "Last Advices and Discoveries of the Master." Dr. Ray W. Spalding, Boston, will be toastmaster at the commemorative banquet Monday, 8 p. m. At the same time on Tuesday a buffet supper, followed by a clinical session and case presentations, is scheduled. Laymen are invited to the combined banquet of the American Institute of Homeopathy and other societies Wednesday at 7 p. m.

FLORIDA

State Medical Meeting at St. Petersburg.—The 81st annual meeting of the Florida Medical Association will convene at the Vinoy Park Hotel, St. Petersburg, April 4-6. The session will be called to order by Dr. Duncan T. McEwan, Orlando, president. Addresses of welcome will be made by Samuel G. Johnson, mayor of St. Petersburg, and Dr. Clyde O. Anderson, St. Petersburg, president, Pinellas County Medical Society. The first scientific assembly will open at 9:45 a. m. Monday with an address "What Is Your A. M. A.?" by Dr. Elmer Hess, Erie, Pa., President-Elect, American Medical Association. At 11:30 a. m. Dr. Alton Ochsner, William Henderson Professor of Surgery and chairman, department of surgery, Tulane University of Louisiana School of Medicine, New Orleans, will discuss "Carcinoma of the Stomach: A Need for Earlier Diagnosis." The afternoon session will be opened at 2 p. m. by Dr. Peter B. Wright, department of orthopedic surgery, Medical College of Georgia, Augusta, who will have as his subject "Emergency Treatment of the Injured." At 11:30 a. m. Tuesday Dr. Claude J. Hunt, Kansas City, Mo., will deliver the invitational address, "Gallbladder Problems." At 2 p. m. there will be a symposium, "The Relationship of Nutrition in Pregnancy to the Newborn," under the sponsorship of the Florida Obstetric and Gynecologic Society and Florida Pediatric Society, with Drs. Harold G. Nix, Tampa, president of the former, and Lewis T. Corum, Tampa, president of the latter, as co-moderators. Dr. Winslow T. Tompkins, associate professor of obstetrics and gynecology, University of Pennsylvania Graduate School of Medicine, Philadelphia, and Dr. Jerome S. Harris, chairman of the pediatric department of the Duke University School of Medicine and Duke Hospital, Durham, N. C., will be collaborators. On Wednesday at 9:30 a. m. Dr. George E. Morris, assistant clinical professor of dermatology, Tufts College Medical School, Boston, will discuss "Contact Dermatitis." A patio party, Tuesday, 6 p. m., will include a fellowship and cocktail hour, immediately preceding the annual dinner, at which Dr. Edward R. Annis, Miami, will serve as master of ceremonies.

Numerous specialty groups will meet during the convention, as will the woman's auxiliary. Dr. Morris will discuss industrial dermatoses at the meeting of the Florida Association of Industrial and Railway Surgeons Tuesday. Dr. Wright will be the speaker for the Florida Orthopedic Society. At the meeting of the Florida chapter, American College of Surgeons, Sunday, Dr. Ochsner will have as his subject "The Treatment of the Postthrombophlebitic Syndrome." Other out-of-state speakers at the specialty meetings include Dr. Maurice G. Buckles,

Columbus, Ohio, who will discuss "Mitral and Aortic Valvuloplasty" before the Florida chapter of the American College of Chest Physicians Sunday afternoon; Dr. Harold G. Scheie, Philadelphia, and Dr. Lester A. Brown, Atlanta, Ga., who will read papers before the Florida Society of Ophthalmology and Otolaryngology; and Dr. Mark M. Marks, Kansas City, Mo., who has been invited to present "Mechanical Aids in Proctologic Teaching" at the meeting of the Florida Proctologic Society Saturday.

ILLINOIS

Psychiatric Lectures.—In its second series on treatment in psychiatry, the North Shore Health Resort (225 Sheridan Road, Winnetka) offers a lecture, "The Value of Emotional Support and Environmental Manipulation," by Dr. Raymond W. Waggoner, professor and chairman of the department of psychiatry, University of Michigan Medical School, Ann Arbor, Mich., April 6, 8 p. m., at the health resort.

Clinics for Crippled Children.—The University of Illinois division of services for crippled children has scheduled the following clinics, to which any private physician may refer or bring any children for whom he may want examination or consultative services:

April 5, Quincy, Blessing Hospital.
April 6, Hinsdale, Hinsdale Sanitarium and Hospital.
April 12, Peoria, Children's Hospital; East St. Louis, Christian Welfare Hospital; Flora, Clay County Hospital.
April 14, Springfield, St. John's Hospital; Cairo, Public Health Building; Elmhurst (rheumatic fever), Memorial Hospital of Du Page County.
April 15, Chicago Heights (rheumatic fever), St. James Hospital.
April 19, Danville, Lake View Hospital.
April 20, Alton (rheumatic fever), Alton Memorial Hospital; Chicago Heights, St. James Hospital.
April 21, Rockford, St. Anthony Hospital; Watseka, American Legion Home.
April 22, Chicago Heights (rheumatic fever), St. James Hospital.
April 26, Peoria, Children's Hospital; Effingham (rheumatic fever), St. Anthony's Emergency Hospital; East St. Louis, St. Mary's Hospital.
April 27, Springfield (cerebral palsy), Memorial Hospital; Elgin, Sherman Hospital.
April 28, Bloomington (general and cerebral palsy), St. Joseph's Hospital; Mt. Vernon, Masonic Temple.

Chicago

Lectures on Medical History.—Under the chairmanship of Dr. Piero P. Foa the Chicago Medical School (710 S. Wolcott Ave.) offers the following lecture series on the evolution of medicine by Ilza Veith, Ph.D., assistant professor, history of medicine, University of Chicago, Tuesdays, 12:30 p. m. in Amphitheatre A:

April 5, The Dawn of Medicine.
April 12, Greek Medicine.
April 19, Medieval Medicine.
April 26, Renaissance Medicine.
May 3, The Beginnings of Modern Medicine.
May 17, Modern Medicine.

Memorial Lecture.—At the meeting of the Illinois Chapter, American College of Chest Physicians, April 8, in the St. Clair Hotel (162 E. Ohio St.) the annual memorial lecture will be delivered by Dr. Andre Cournand, director of the cardiopulmonary laboratory, Bellevue Hospital, New York, who will discuss "The Physiologic Basis of Treatment of Chronic Diffuse Pulmonary Emphysema." The scientific session at 8 p. m. will be preceded by a fellowship hour (6 p. m.) and dinner (7 p. m.). Members of the American College of Chest Physicians are welcome to attend a talk by Dr. Cournand at Cook County Children's Amphitheater Friday at 11 a. m., when his subject will be "Recent Developments in the Problem of the Control of Pulmonary Circulation in Man."

Conference on Nutrition.—A conference on optimal nutrition, its analysis and application will be held April 8-9 at George Williams College (Drexel at 53rd St., Chicago 15) under the cosponsorship of the college and the Rehabilitation Institute of Chicago. Friday afternoon Dr. Harold M. Sterling, medical director, and Genevieve Anthony, dietitian, Illinois Children's Hospital-School (department of public welfare, state of Illinois), will present "Clinical Experiences with Optimal Nutrition in Severely Handicapped Children," with a supplementary report, "Experience with Amino Acids and Exercise in the Treatment of Muscular Dystrophy in a Boy: A Case History," by Dr. Edwin C. Welsh, clinical instructor, department of physical medicine, Marquette University School of Medicine, Milwaukee. Saturday morning will be devoted to a symposium "Some Clinical Observations on Optimal Nutrition and Resistance to Toxic Factors," which will include the following presentations by physicians:

James M. Devereux, Parsons, Kan., A Controlled Study of 50 Employees Affected by Toxic Influence of Handling TNT.
Jack C. Cooper, Houston, Texas, A Study of Chronic Alcoholism at the City Prison Farm, Houston, Texas.
W. Everett Glass, Taunton, Mass., Experiences in the Treatment of Delirium Tremens with Optimal Nutrition.
Ruth Fox, New York, Supplementary Nutrition as an Adjunctive Therapy in Alcohol Patients.
R. Gordon Bell, Ontario, Canada, Possible Role of Protein Malnutrition in Chronic Alcoholism.

Other presentations during the conference include:

Paul R. Cannon, Chicago, Intracellular Ions in Relation to Protein Synthesis.
Lt. Col. Curtis P. Artz, Houston, Texas, Extension of Oral Feeding at Optimal Levels in the Management of Burns and Injuries.
Ben L. Boynton, Chicago, Some Unexpected Results from Rehabilitation Procedures Supported by a Program of Optimal Nutrition.

At the dinner session Friday, 6:45 p. m., in the Quadrangle Club (1155 E. 57th St.), Dr. Angus M. Thomson, University of Aberdeen, Aberdeen, Scotland, will present "The Diagnosis of Malnutrition in Man." The conference will close with an address, "The Protein Factor in Optimal Nutrition," by Dr. Willard A. Krehl, Ph.D., associate professor, department of nutrition, Yale University School of Medicine, New Haven, Conn. Anton J. Carlson, Ph.D., is honorary chairman of the conference committee, and Arthur H. Steinhaus, Ph.D., is chairman.

KENTUCKY

Officers Conference at Lexington.—The fifth annual County Society Officers Conference will convene at the Phoenix Hotel, Lexington, April 7. Dr. Ernest B. Howard, Chicago, Assistant Secretary of the American Medical Association, will deliver an address entitled "How the A. M. A. Serves You and the Public." Dr. Walter L. Portteus, Franklin, Ind., president of the Indiana State Medical Association, will talk on the practical physician-patient relations in such fields as fees and statements. Dr. C. Elliott Bell, Decatur, Ill., will have as his subject "The Vertical Approach to Community Influence." Other features of the conference will include a panel presented by representatives of the various counties, featuring some outstanding projects. A half-hour movie, suitable for use on television, will be shown before the conference.

MASSACHUSETTS

Lecture by Dr. Pack.—At the Worcester District Medical Society meeting April 13 in the Worcester Medical Library Hall (rear of 57 Cedar St., Boston) Dr. George T. Pack, New York, will speak on the definition of adequate surgery in the treatment of cancer.

Postgraduate Course in Obstetrics and Pediatrics.—On April 7-9 Boston Lying-In Hospital and Children's Medical Center, in cooperation with the Massachusetts department of public health, will offer, without charge, a postgraduate course in obstetrics and pediatrics for physicians. Recent advances in the medical care of the pregnant woman, the newborn infant, and the neonatal infant will be presented in an intensive program of lectures, conferences, clinical demonstrations, ward rounds, and clinicopathological conferences. Application for the course should be made to Dr. Crawford H. Hinman, 1180 Beacon St., Brookline.

MICHIGAN

Society News.—Dr. Samuel F. Marshall, Lahey Clinic, Boston, will discuss abdominal tumors before the meeting of the Wayne County Medical Society, April 4. His lecture, at the Wayne University Medical School Auditorium at 8:30 p. m., will be preceded by a subscription dinner at the David Whitney House.

Course on Clinical Electrocardiography.—A course on clinical electrocardiography will be given April 11-15 in the auditorium of Wayne University College of Medicine (645 Mullett St.,

Detroit), with Dr. Gordon B. Myers as director. The course, arranged by the American College of Physicians, will have as officers of instruction members of the faculty of Wayne University College of Medicine. The fee for ACP members is $30; for nonmembers, $60.

Cancer Day.—The Genesee County Medical Society will hold its 10th annual cancer day April 13 in the Merliss Brown Auditorium, Hurley Hospital, Flint. At 9:30 a. m. an address of welcome will be delivered by Dr. Ernest P. Griffin, Flint, president of the society. Dr. Robert H. Baker, Pontiac, president of the Michigan State Medical Society, will preside over the morning program:

Prognosis of Cancer from the Viewpoint of the Surgical Pathologist, Lauren V. Ackerman, St. Louis.
Outstanding Indications and Possibilities of Radiotherapy in the Treatment of Cancer, Juan A. del Regato, Colorado Springs, Colo.
Vertebral Venous Function and Its Role in the Spread of Cancer, Oscar V. Batson, Philadelphia.

At 12:45 p. m. luncheon will be served in the lobby floor cafeteria, after which Dr. Grantley W. Taylor, Harvard Medical School and Massachusetts General Hospital, Boston, will preside over the afternoon session:

Present Status of the Treatment of Pulmonary Cancer, Brian B. Blades, Washington, D. C.
Place of Chemotherapy in the Management of Leukemia, Frank H. Bethell, Ann Arbor, Mich.
Ten Years of Progress with the Cancer Problem, Cornelius P. Rhoads, New York.

At 4 p. m. Dr. Taylor will moderate a panel discussion of current cancer problems, in which the day's speakers will participate. A social hour, 5:30 p. m., will precede a subscription dinner, 7 p. m., at the Durant Hotel.

NEW YORK

Society News.—"Recent Studies of Neonatal Mortality" will be the subject of a talk by Dr. Edith L. Potter, associate professor of pathology (obstetrics and gynecology), University of Chicago School of Medicine, before the Rochester Academy of Medicine (1441 East Ave.) at 8:30 p. m., April 5.

Public Forum.—"You and Your Health" is the theme of the public forum that will be presented in White Plains by the Westchester Academy of Medicine and the Medical Society of the County of Westchester. Session topics will be:

April 11, You and Your Heart.
April 18, You and Cancer.
April 25, You and Your Nerves.
May 2, Your Child and Polio.

Cancer Conference.—The seventh meeting of the New York Cancer Society (Sixth National Gastrointestinal Cancer Conference) April 4-5 in Hosack Hall, New York Academy of Medicine, will be sponsored by the Gastrointestinal Cancer Committee of the National Advisory Cancer Council, National Cancer Institute, Public Health Service, U. S. Department of Health, Education, and Welfare. Dr. George T. Pack, New York, will deliver the address of welcome Monday at 9 a. m., preceding introductory remarks by Dr. John R. Heller, director, National Cancer Institute, Bethesda, Md. The following presentations will be made on Monday:

Incidence and Behavior of Gastric Cancer, T. H. Crawford Barclay, Regina, Saskatchewan, Canada.
Role of Heredity in Gastric and Intestinal Cancer, Madge T. Macklin, Columbus, Ohio.
Failures in Diagnosis of Gastric Cancer, Robert C. Horn Jr., Philadelphia.
Natural History of Survival in Carcinoma of the Stomach, Treated and Untreated, H. Marvin Pollard, Ann Arbor, Mich.
Gastric Malignant Lymphoma: Increasing Accuracy in Diagnosis, Melvin I. Klayman, Chicago.
Use of Image Tubes and Amateur Photographic Equipment to Reduce Exposure to Radiation at Fluoroscopy, W. Edward Chamberlain, Philadelphia.
An Evaluation of the Sources of Error in Roentgenologic Diagnosis of Neoplasma of the Small Intestine, Theodore E. Keats, San Francisco.
Diagnosis of Gastric Malignancy in Pernicious Anemia, Cyrus E. Rubin, Seattle.
Cytology in Diagnosis and Investigation of Gastric Cancer, Norman Zamcheck, Boston.
Clinical Significance of the Electrogastrogram, Edmund N. Goodman, New York.
Gastric Ulcer Problem, Mark A. Hayes, New Haven, Conn.

The sessions will end Tuesday, 12:30 p. m., with a general discussion after the following program:

Value of Achlorhydria as a Screening Test for Gastric Cancer: A 10-Year Report, Claude R. Hitchcock, Minneapolis.
Present Status and Trend of Ion Exchange Tubeless Determinants of Gastric Acidity, Harry L. Segal, Rochester, N. Y.
Clinical Use of the Urinary Uropepsin Excretion in Distinguishing Benign Form Malignant Gastric Cancer, Seymour J. Gray, Boston.
Differentiation of Achylia Gastrica and Achlorhydria by Means of Radioactive Vitamin B_{12}, Lloyd D. MacLean, Minneapolis.
Intestinal Absorption of Radioactive Vitamin B_{12} in Patients with Cancer of the Stomach Following Subtotal and Total Gastrectomy, G. B. Jerzy Glass, New York.

New York City

Research in Enzyme Chemistry.—The Rockefeller Foundation has given the New York University–Bellevue Medical Center a gift of $100,000 for support of research in the field of cellular enzyme chemistry under the direction of Dr. Severo Ochoa, chairman, department of biochemistry, New York University College of Medicine, a unit of New York University–Bellevue Medical Center. About half of the grant will be used for the purchase of equipment; the remainder will help finance the research project over a seven year period. During the past 10 years, Dr. Ochoa has led a research group at the medical center that has investigated chemical reactions that convert food to energy inside the living cell. His study is one of the about 1,500 closely coordinated research projects currently conducted by New York University–Bellevue Medical Center, where the research budget for the current year is $2,400,000.

NORTH CAROLINA

Psychiatric Center.—The Psychiatric Outpatient Center of the North Carolina Memorial Hospital, Chapel Hill, was opened for inpatient and outpatient services Jan. 10. It offers diagnostic, treatment, and consultation services for children and adults. Primarily established to serve in-state patients, it serves out-of-state patients when suitable arrangements can be made. Appointments can be made by contacting the director.

Seventy-Fifth Anniversary.—The University of North Carolina School of Medicine has planned an elaborate program (April 12-13) to celebrate the 75th anniversary of the beginning of medical education at Chapel Hill. Dr. William P. Richardson is head of the special committee completing plans for the event. The program opens Tuesday evening with a panel, "The State University and Medical Care in the State," moderated by Major L. P. McLendon, Greensboro. Wednesday morning Joseph C. Hinsey, Ph.D., dean of Cornell University Medical College, New York, will be moderator for a panel on the general topic, "Financing Medical Education." Wednesday afternoon Everett W. Hall, Ph.D., of the department of philosophy will be moderator of the panel, "Humane Letters and Human Illness." The panels will be presented in Hill Music Hall. The alumni meeting will be held at dinner Wednesday evening in Lenoir Hall.

OHIO

Symposium on Industrial Medicine.—On April 5 the Academy of Medicine of Cincinnati will present a symposium, "Industrial Problems in Medicine," by Dr. Rutherford T. Johnstone, clinical professor of medicine (industrial), University of California, Los Angeles; Dr. W. P. Shepard, New York, chairman, Council on Industrial Health, American Medical Association; and the moderator, Dr. Robert A. Kehoe, professor and director, department of preventive medicine and industrial health, University of Cincinnati College of Medicine.

PENNSYLVANIA

Dr. Mattison Named State Health Secretary.—Dr. Berwyn F. Mattison, commissioner of health of Erie County, N. Y., since 1948, recently became secretary of health in Governor Leader's cabinet, succeeding Dr. Russell E. Teague who returned to active duty with the U. S. Public Health Service in Washington. Before 1948 Dr. Mattison served with the New York state health department as assistant district health officer, district state health officer, and commissioner of health in Yonkers.

Philadelphia

Lecture by Dr. Priscilla White.—The Mu chapter of Phi Delta Epsilon Fraternity at Jefferson Medical College of Philadelphia will sponsor the eighth annual lectureship on April 4 at 8:15 p. m., at which time Dr. Priscilla White of the Joslin Clinic, Boston, will discuss "Pregnancy Complicating Diabetes." The lecture, which will be held in the McClellan Hall of the college, is open to the medical profession.

Personal.—Dr. Charles F. McKhann was guest of honor at the annual assembly of the section on pediatrics, Puerto Rico Medical Association. Dr McKhann, who is professor of pediatrics and head of the department at Jefferson Medical College of Philadelphia, conducted seminars on nephrosis in children and on inborn errors of metabolism, lectured on recent advances in pediatrics, and conducted a conference on craniosynostosis and subdural fluids in young children.

Jefferson Hospital Pavilion.—Vice-Admiral James L. Kauffman, U. S. N. (retired), president of Jefferson Medical College and Hospital, recently presided over the opening ceremonies at Jefferson Medical College Hospital's new 14 story, 300 bed, $7,500,000 pavilion (11th Street between Walnut and Sansom streets). The principal speaker was Dr. Frank R. Bradley, superintendent of Barnes Hospital, St. Louis, and president of the

New Pavilion at Jefferson Medical College Hospital.

American Hospital Association. Attached to the Thompson Annex, the pavilion will accommodate about 8,500 additional patients yearly and enable the hospital to serve more than 30,000 bed patients annually. Of the seven nursing floors, one is devoted exclusively to maternity patients, with optional "rooming in" maternity service. All the surgical work of the hospital will be centralized in the 14 operating rooms on two floors of the new building. Expanded radiology and clinical laboratories also occupy individual floors. Another floor for gynecology and obstetrics includes four operating rooms, four delivery rooms, and three labor rooms. Dr. Hayward R. Hamrick, vice-president of the college, is medical director.

TENNESSEE

Personal.—Dr. James W. Davis, Chattanooga, Alton Ochsner Medical Foundation fellow-in-surgery, recently received the foundation's annual award of $100 and a certificate for excellence in medical writing. The subject of his thesis was "The Lymphatic Drainage of the Lungs, with Special Reference to the Right Upper Lobe."

Neurologist Added to Faculty.—The University of Tennessee College of Medicine, Memphis, has appointed its first full-time neurologist, Dr. Gene M. Lasater, who currently serves as an instructor in the division of neurology, University of Minnesota Medical School, Minneapolis, Dr. Lasater, who on July 1 will become assistant professor in the department of neurology and psychiatry, served as chief of the neurological section of the Fifth General Hospital, U. S. Army Medical Corps, in Stuttgart, Germany, from 1951 to 1953, when he took his present position.

TEXAS

Tumor Conference.—The fourth annual State Tumor Conference, April 6, in Wichita Falls in the main auditorium of Midwestern University will be sponsored by the Wichita County Medical Society Tumor Clinic, the Texas State Department of Health, and the American Cancer Society. There is no registration fee. The conference is approved for formal postgraduate training. The program will open with an address of welcome by Dr. Roger W. Manar, Wichita Falls, president, Wichita County Medical Society. Speakers will include:

Mandred W. Comfort, Rochester, Minn., Early Detection of Cancer. Early Diagnosis of Cancer and the Survival Rates.
Charles W. Mayo, Rochester, Minn., Carcinoma of the Colon and Rectum. End Results of Treatment of Cancer of the Colon and Rectum.
Manuel M. Garcia, New Orleans, Scope and Effectiveness of Modern Radiotherapy for Cancer. Treatment of Head and Neck Cancer by Irradiation.

WASHINGTON

Surgical Meeting in Spokane.—The 18th annual meeting of the Spokane Surgical Society will be held at the Davenport Hotel, April 2, under the presidency of Dr. Richard D. Reekie, Spokane. The guest speaker, Dr. Norman F. Miller, Bates Professor and chairman of the department of obstetrics and gynecology, University of Michigan hospital, Ann Arbor, will deliver an address, "Uterine Fibroids," at the noon luncheon. His paper, "Urinary Incontinence in the Female," will close the afternoon session, which will begin at 2 p. m. with a symposium on back pain. At the banquet (informal) 7 p. m., he will have as his subject "Surgical Restorations of the Relaxed Perineum."

WEST VIRGINIA

Society News.—At the recent annual meeting of the West Virginia Heart Association, Dr. Francis J. Gaydosh, Wheeling, was elected president; Dr. William E. Bray Jr., Huntington, president-elect; Dr. James R. Shanklin, Bluefield, vice-president; Dr. James H. Wolverton Jr., Piedmont, secretary; and Mr. R. E. Plott, Charleston, treasurer (reelected).

General Practice Meeting in Charleston.—The third annual scientific assembly of the West Virginia Academy of General Practice will be held at the Daniel Boone Hotel in Charleston April 16-17 under the presidency of Dr. T. Maxfield Barber, Charleston. Dr. Louis H. Bauer, Hempstead, N. Y., past President of the American Medical Association and now secretary-general of the World Medical Association, will be speaker at the banquet Saturday, 7:15 p. m. His subject will be "World Status of the General Practitioner." The meeting will open at 9:15 a. m. with "Certain Aspects of Hypothyroidism in Childhood" by Dr. Weston M. Kelsey, Winston-Salem, N. C., followed by "Care of Premature Infants" by Dr. Richard L. Day, New York, and "The Practice of Pediatrics by the General Practitioner" by Dr. Waldo E. Nelson, Philadelphia. The following program will be presented Saturday afternoon:

The Acute Leukemias, Charles A. Doan, Columbus, Ohio.
Diagnosis of Various Acute Nontubercular Pulmonary Infections, Theodore E. Woodward, Baltimore.
Study of the Basic Mechanism of Rheumatic Diseases, Thomas McPherson Brown, Washington, D. C.
Chronic Rheumatoid Arthritic: Total Rehabilitation, Edward W. Lowman, New York.
Chronic Complications of Diabetes Mellitus, E. Perry McCullagh, Cleveland.
Problems of Libido and Potentia Encountered in General Practice, George Lombard Kelly, Augusta, Ga.
Management of Congestive Heart Failure, E. Hugh Luckey, New York.

The Sunday morning program will include:

Bleeding in the Third Trimester of Pregnancy, F. Bayard Carter, Durham, N. C.
The Study of the Sterile Couple, Morris Edward Davis, Chicago.
Ovarian Carcinoma, Frederick H. Falls, Chicago.

The concluding session, Sunday afternoon, will present:

Acute Abdominal Injuries, Frederick E. Kredel, Charleston, S. C.
Pancreatitis, James Taggart Priestley, Rochester, Minn.
Hyperfunctioning Tumors of the Endocrine Glands, Robert James Coffey, Washington, D. C.
Problems in Diagnosis and Management of Massive Bleeding from the G. I. Tract, Herbert R. Hawthorne, Philadelphia.

There will be a panel discussion and question-and-answer period at the close of each session. All physicians in West Virginia

and nearby states are invited to attend the meeting. Information may be obtained by writing to the chairman of the committee on arrangements, Dr. Halvard Wanger, Shepherdstown.

WISCONSIN

Psychosomatic Forum.—Dr. Isadore I. Cash, speaking before the Milwaukee Psychosomatic Forum at 7:30 p. m., April 6, in the Elks Club, will present "Personality Considerations in the Study of Peptic Ulcer Patients." All physicians are welcome to attend.

Lecture by Dr. Ivan Duff.—The Alpha Omega Alpha fraternity of the University of Wisconsin Medical School, Madison, recently presented a lecture, "Joint Fluid Changes Induced by Systemic and Local Administration of Steroids," by Dr. Ivan F. Duff, director, Rackham Arthritis Research Unit, University of Michigan Medical School, Ann Arbor.

Miller Memorial Lecture.—Phi Beta Pi of the University of Wisconsin presented the William Snow Miller Memorial Lecture, "Philosophy and Medicine," by Dr. Jerome R. Head, assistant professor of surgery, Northwestern University Medical School, Chicago, March 3, in the auditorium of Service Memorial Institute, Madison.

HAWAII

Society News.—The February meeting of the Honolulu County Medical Society had an international flavor. The program included:

United States: Report on Advances in Medicine and Surgery at the University of Chicago, Ralph B. Cloward, Honolulu.
Europe: Report on Advances at the World Medical Congress, Rome, 1954, and the Third International Congress of Chest Diseases, Barcelona, Luther C. Beck, Honolulu.
Carribean: International Training of Health Workers in Puerto Rico, Richard K. C. Lee, Honolulu.
Japan: Radiation Sickness: Acute and Chronic, Katherine J. Edgar, Honolulu.

GENERAL

Cerebral Palsy Grants.—United Cerebral Palsy (369 Lexington Ave., New York) announces that research and training grants to leading universities, hospitals, and institutions totaled more than half a million dollars during its last fiscal year, a record amount in the organization's five-year history. Thirty-five research grants totaling $350,241 were made, as compared with $254,940 during the preceding year. In addition, 19 training grants totaling $172,540 were authorized.

Awards of Tuberculosis Association.—According to Dr. Esmond R. Long, Philadelphia, director of medical research for the American Trudeau Society, 39 grants-in-aid of medical research sponsored by the National Tuberculosis Association and its medical section, the American Trudeau Society, were awarded for the 1954-1955 fiscal year of the association. Sharing in the $200,555 total were 28 physicians. Four medical research fellowships, totaling $14,600, were also approved, as was payment of $2,104 to the National Research Council.

Surgical Scholarship for Foreign Study.—The International College of Surgeons, through the generosity of the Woman's Auxiliary of the United States and Canadian sections, is offering a scholarship to a young Canadian or American surgeon who wishes to study abroad. This is not a traveling fellowship. The physician selected will be expected to spend at least 10 months of the year as a resident or fellow in a teaching center in one of the countries of Europe or South America. The scholarship will be in the amount of $3,000 to pay for transportation and living expenses for 12 months. Details may be obtained from the Scholarship Committee, International College of Surgeons, 1516 Lake Shore Dr., Chicago 10.

Meeting of Pathologists and Bacteriologists.—The American Association of Pathologists and Bacteriologists will hold its 52nd annual meeting at the Hotel Shamrock, Houston, Texas, April 7-9, under the presidency of Dr. G. Lyman Duff, Montreal, Canada. In all, 56 papers will be presented and 12 read by title. By invitation of the council, Dr. Jean R. Oliver, Brooklyn, will act as referee for an all-day symposium, "New Approaches to the Study of Renal Disorders," on Friday. Chauncey D. Leake, Ph.D., executive director, University of Texas Medical Branch, Galveston, will be the speaker at the annual dinner Thursday, 7 p. m., which will be preceded by a reception and fellowship hour. Cost of banquet tickets will be $7. Members of the International Association of Medical Museums, which will hold its meeting immediately preceding that of the association, and guests are cordially invited to attend the reception and the dinner.

United States-Mexico Border Public Health Association.—The 13th annual meeting of the United States-Mexican Border Public Health Association will be held at the Hotel del Bosque, Melchior Ocainpo Num. 323, Mexico, D. F., Mexico, May 6-9. The secretary, Dr. Sidney B. Clark (204 U. S. Court House, El Paso, Texas), invites suggestions for the general sessions. Officers elected at the last annual meeting included: president, Dr. Arturo Rico Gonzalez, Jefe, Servicios Coordinados de Salubridad y Asistencia, Chihuahua, Chih.; president-elect, Mr. George W. Marx, director and chief engineer, Bureau of Sanitation, Arizona State Department of Health, Phoenix, Ariz.; vice-president (U. S.), Dr. Donald G. Davy, assistant director, Division of Local Health Services, California Department of Public Health, San Francisco; vice-president (Mexico), Dr. Francisco Arriola G., Jefe, Unidad Sanitaria, Nogales, Sonora; and secretary-treasurer, Dr. Sidney B. Clark, Pan American Sanitary Bureau, El Paso, Texas.

Northern Tri-State Meeting.—The 82nd annual meeting of the Northern Tri-State Medical Association will open in the Chamber of Commerce Building, Fort Wayne, Ind., at 9:30 a. m., April 5. Addresses of welcome by the association's president, Dr. Thomas D. Armstrong, Michigan City, Ind., and by Dr. Arthur J. Roser, Fort Wayne, Ind., president, Allen County Medical Society, will precede a presentation, "Varicose Veins," by Dr. Thomas T. Myers, Mayo Clinic, Rochester, Minn., who will later speak on the postphlebitic leg. Other presentations by physicians include "Kidney Disease," by Dr. Robert M. Kark, professor of medicine, University of Illinois College of Medicine, Chicago, and "Carcinoma of the Colon," by Dr. Leon J. Witkowski, associate professor of surgery, Northwestern University Medical School, Chicago. Attorney Albert Stump, Indianapolis, legal counselor for the Indiana State Medical Association, will speak on current medical legal problems.

Meeting on Cardiac Pathology.—The 44th annual meeting of the International Association of Medical Museums will be held at the Hotel Shamrock, Houston, Texas, April 5-6, just preceding the meeting of the American Association of Pathologists and Bacteriologists. By special invitation of the council a course in pathological physiology and pathology of the heart will be presented Tuesday afternoon and all day Wednesday. Dr. Jesse E. Edwards, professor of pathological anatomy, Mayo Foundation, Rochester, Minn., will serve as moderator. To afford an opportunity for observation at close range of the exact steps and methods used in certain techniques, the following demonstrations have been arranged: permanent frozen section; methods of tumor transplantation in animals; periodic acid-Schiff and related mucopolysaccharide stains; stains for micro-organisms and fungi in tissue; illustrative material for lectures and conferences; gross examination of the heart; and histochemical reactions for nucleic acid.

Kimble Methodology Research Award.—Nominations are now being accepted for the fourth Kimble Methodology Research award, which will be presented in November through the generosity of the Kimble Glassware Division of Owens-Illinois Co. The award ($500 and a suitably inscribed plaque) is administered by committees of the Conference of State and Provincial Public Health Laboratory Directors. To be eligible for consideration for nomination in 1955, the work should have been completed since Jan. 1, 1950, and should be accompanied by a reprint or a summary with bibliography and a statement of the considerations that justified the recommendation of the study; candidates should be from the United States, its territories, or Canada; and the work should be either a fundamental con-

tribution that serves as a base line for development of diagnostic methods that fall within the province of the public health laboratory or the adaptation of a fundamental contribution to make it of use in a diagnostic laboratory. Nominations received after May 30 will not be considered for the Kimble Methodology Research Award for 1955 but will be considered for nomination in 1956, providing the work was completed since Jan. 1, 1951. Nominations should be sent to M. Scherago, D.V.M., Chairman, Nominating Committee, Kimble Methodology Research Award, Department of Bacteriology, University of Kentucky, Lexington.

Scholarships in Plastic Surgery.—The Foundation of the American Society of Plastic and Reconstructive Surgery announces its 1955 scholarship contests. In the junior classification the contest is restricted to residents in training and to plastic surgeons who have been in practice no longer than five years. Essayists must be residents of the American continent, British dominions, or Western Europe. Two prizes ($1,000 and a three month scholarship, and $750 and a three month scholarship) are offered for essays (about 5,000 words) that are the result of some original research (either clinical or experimental) in plastic and reconstructive surgery. Papers that have been previously published (even in part) will not be accepted. All essays must be submitted in quadruplicate, and in English only, with no indication of the writer's name or institutional affiliation. An additional envelope shall include the contestant's name, address, and institutional affiliation, with details of professional training and percentage of practice in plastic surgery. Character references must be forwarded by two leading plastic surgeons from the applicant's country. Contestants in the senior classification must have been in active practice of plastic and reconstructive surgery for more than five years. A silver plaque or certificate of honorable mention is offered for a winning essay in this classification. Requirements are the same as those for the junior classification. Manuscripts will not be accepted by the award committee after July 1. The winning essays must be presented in person at the annual meeting of the American Society of Plastic and Reconstructive Surgery in Atlantic City, Sept. 25-30. Information may be had by writing to the Award Committee, % the Foundation of the American Society of Plastic and Reconstructive Surgery, Inc., 30 Central Park South, New York 19.

Fulbright Awards.—Announcement is made of the United States government awards for the academic year 1956-1957, authorized under the Fulbright act and presented under the auspices of the Department of State and the Board of Foreign Scholarships. Awards are available for university lecturing and advanced research in Australia (March-December, 1956); Burma (June, 1956-March, 1957); Ceylon (June, 1956-March, 1957); India, subject to availability of funds (July, 1956-April, 1957); New Zealand (March-December, 1956); the Philippines (June, 1956-April, 1957); and Thailand (May, 1956-April, 1957). Applicants must be United States citizens. Those applying for lectureships are expected to have at least one year of college or university teaching experience in the United States or abroad. Applicants for research awards are expected to have a doctoral degree from a recognized institution of higher learning in the United States or abroad at the time of application, or recognized standing in their respective professions. Candidates for the doctoral degree or those expecting to obtain it in the normal course of their training should apply to the Institute of International Education, 1 E. 67th St., New York. To insure consideration, applications must be postmarked no later than April 15. The 1956-1957 programs for Austria, Belgium and Luxembourg, Denmark, Finland, France, Germany, Greece, Iraq, Italy, Japan, Netherlands, Norway, the United Kingdom and colonial dependencies, and, subject to the availability of funds, for Egypt, Pakistan, and Sweden will be announced in July, although applications will be accepted from May 1 through the closing date, Oct. 1, 1955. Application forms and additional information are obtainable from the Conference Board of Associated Research Councils, Committee on International Exchange of Persons, 2101 Constitution Ave., Washington 25, D. C.

Railway Surgeons Meet in Chicago.—The 67th annual meeting of the American Association of Railway Surgeons will be held at the Drake Hotel April 12-14 under the presidency of Dr. William G. Bessmer, Davenport, Iowa. The following presentations have been scheduled:

Dermatitis in the Railroad Industry, John B. Haeberlin Jr., Chicago.
Changing Concepts in Bowel Obstruction, William C. Beck, Sayre, Pa.
Treatment of Fractures of Upper Tibia, Willis K. West, Oklahoma City.
Hazards of Radiation, Paul W. Greeley, Chicago.
Hypersplenism and the Anemias, Steven O. Schwartz, Chicago.
The Gallbladder Problem, Claude J. Hunt, Kansas City, Mo.
Methods and Principles in Skin and Soft Tissue Transplantation, A. Neal Owens, New Orleans.
Trauma and the Psychiatrist, John R. Adams, Chicago.
Therapy of Hypertension, LeRoy H. Sloan, Chicago.
Surgery of the Kidney in Cardiovascular Disease, George J. Bulkley, Chicago.
Diagnosis and Treatment of Coronary Thrombosis, Don C. Sutton, Chicago.
Status of the Surgical Treatment of Hypertension and Peripheral Vascular Disease, Adrien H. Verbrugghen, Chicago.
Carcinoma of the Breast, Carl W. Eberbach, Milwaukee.
Management of Multiple Injuries, John L. Lindquist, Chicago.
Fractures of the Upper End of the Femur, James J. Callahan, Chicago.
Traffic Injuries—A Surgical Problem, Richard W. Zollinger, Columbus, Ohio.
Principles of Rehabilitation, Ben L. Boynton, Chicago.
Traumatic Lesions of the Chest, Willard Van Hazel, Chicago.
Surgical Treatment for Diverticulosis of the Colon, Edward S. Judd, Rochester, Minn.
Diagnosis and Treatment of Hemorrhoids, Guy V. Pontius, Chicago.

A fellowship hour, Wednesday, 6:30 to 7:30 p. m., will precede the annual dinner (informal) at which the toastmaster will be Dr. Bessmer and the speaker, Mr. Arthur Briese, Hot Springs, Ark., whose topic will be "Skulduggery at the Old Cross Roads." Ladies and guests are invited.

CANADA

Symposium on Modern Trends in Treatment.—On April 4 at the Royal Alexandra Hotel, Winnipeg, the Manitoba Medical Association and the committee for postgraduate studies, Faculty of Medicine, University of Manitoba, together with Lederle Laboratories, will sponsor the following symposium on modern trends in treatment:

Problems in the Management of Juvenile Diabetes, Andrew L. Chute, Toronto.
Modern Treatment of Hypertension, Kenneth A. Evelyn, Montreal.
Chemotherapy of Malignant Disease, Olof H. Pearson, New York.
Recent Advancements in Cardiac Surgery, Charles B. Ripstein, New York.
Recent Advancements in the Treatment of Allergic Disorders, Bram Rose, Montreal.
Indications for Hysterectomy, Richard W. TeLinde, Baltimore.

All interested physicians and their wives are invited to this meeting. There will be no registration fee, and at noon physicians and their wives will be guests at luncheon. At 5:30 p. m. there will be a reception. On Tuesday, Wednesday, and Thursday, the Faculty of Medicine, University of Manitoba, will present its annual refresher course at the Winnipeg General Hospital and the Medical School. It is expected that some of the speakers at the Monday symposium will speak at the Tuesday sessions of the refresher course, but there will be a change of topics.

FOREIGN

Commemorative Postmark.—A special commemorative postmark has been authorized for the 16th General Assembly of the International Pharmaceutical Federation. Stamp collectors can have a specimen of the postmark by sending an addressed envelope and an international reply-paid coupon to the secretary of the federation's organizing committee at 17 Bloomsbury Square, London, W. C. 1. The congress, which is being organized by the Pharmaceutical Society of Great Britain, will be held in London, Sept. 19-23.

Science Days.—An International Symposium on Problems of Scientific Research will be sponsored by the National Research Council of Italy at the National Museum of Science and Technology, Milan, April 12-14, during the fifth session of the science days. The general subjects to be considered include: freedom and responsibilities of scientific research; scientific research in universities; training of research workers and their position; scientific research and technical progress; administrative outline of scientific research; scientific research and industry; and fundamental and applied research.

Seminar Congresses in Dermatology and Syphilology.—In its seminar congresses in dermatology and syphilology the American Medical Society of Vienna will present the following programs by the medical faculty of the University of Vienna:

May 9-11, Dermopathology; Dermatologic Histopathology; Demonstrations.
July 11-13, Superficial Mycoses; Deep Mycoses; Demonstrations.
Sept. 12-14, Burns; Dermatology; Demonstrations.
Nov. 7-9, Syphilology; Allergic Skin Diseases; Demonstrations.

Details may be obtained from the American Medical Society of Vienna, Universitaetsstrasse 11, Vienna 1, Austria. Cable: "Ammedic" Vienna.

Symposium on Public Health Problems.—The Austrian chapter of the International Society of Preventive Medicine will hold a symposium on the prevention, diagnosis, and treatment of important public health problems from a sociohygienic point of view, in Pörtschach on Wörthersee (Carinthia), Austria, May 25-28. The topics to be considered include (1) new developments in social and industrial medicine, (2) prevention of infectious diseases, with special emphasis on poliomyelitis, (3) gerontology and metabolic ailments, and (4) prevention of cardiovascular diseases. Medical and pharmaceutical exhibitions and the showing of new medical motion pictures will be added features. Information may be obtained from Dr. M. Arthur Kline, Executive Secretary, the American Medical Society of Vienna, Universitaetsstrasse 11, Vienna 1, Austria.

Middle East Medical Assembly.—The fifth Middle East Medical Assembly will convene April 22-24 at the American University of Beirut, Lebanon, under the auspices of the medical school and the medical alumni and the chairmanship of Dr. John L. Wilson, professor of surgery. Presentations and discussions will cover subjects of practical value to physicians of the Middle East. Among the speakers from the United States will be: Drs. Allen O. Whipple, Frank B. Berry, and R. Townley Paton, New York; Dr. Robert B. Brown, Bethesda, Md.; Drs. Sara M. Jordan and Claude E. Welch, Boston; Drs. Raymond W. McNealy and Harold A. Sofield, Chicago; Dr. Bernard Soderberg, U. S. Army, Europe; Dr. Robert J. Hoagland, U. S. Army, Heidelberg, Germany; Dr. Cecil J. Watson, Minneapolis; and Dr. Dwight L. Wilbur, San Francisco. Symposiums have been arranged on trauma, ophthalmology, urology, and gastroenterology. A panel on psychosomatic medicine has also been scheduled.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1955 Annual Meeting, Atlantic City, N. J., June 6-10.

1955 Clinical Meeting, Boston, Nov. 29-Dec. 2.

1956 Annual Meeting, Chicago, June 11-15.

1956 Clinical Meeting, Seattle, Nov. 27-30.

1957 Annual Meeting, New York, June 3-7.

ALABAMA, MEDICAL ASSOCIATION OF THE STATE OF, Whitley Hotel, Montgomery, April 21-23. Dr. Douglas L. Cannon, 537 Dexter Ave., Montgomery, Secretary.

AMERICAN ACADEMY OF NEUROLOGY, Shamrock Hotel, Houston, Tex., April 28-30. Dr. Alexander T. Ross, Indiana University Medical Center, Indianapolis 7, Secretary.

AMERICAN ACADEMY OF PEDIATRICS, Spring Session, Sheraton-Cadillac Hotel, Detroit, April 4-7. Dr. E. H. Christopherson, 610 Church St., Evanston, Ill., Executive Secretary.

AMERICAN ASSOCIATION OF ANATOMISTS, Philadelphia, April 6-8. Dr. N. L. Hoerr, 2109 Adelbert Rd., Cleveland 6, Secretary.

AMERICAN ASSOCIATION FOR CLEFT PALATE REHABILITATION, Statler Hotel, Boston, May 13-14. Dr. Jack Matthews, 1617 Cathedral of Learning, University of Pittsburgh, Pittsburgh 13, Secretary.

AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS, Monterey Lodge, Monterey, Calif., May 22-25. Dr. John A. Taylor, 2 East 54th St., New York 22, Secretary.

AMERICAN ASSOCIATION FOR HEALTH, PHYSICAL EDUCATION AND RECREATION, Hotel Statler, Boston, April 17-20. Mr. William F. Meredith, Dept. of Physical Education, University of Pennsylvania, Philadelphia 4, Secretary.

AMERICAN ASSOCIATION OF THE HISTORY OF MEDICINE, Hotel Park Shelton, Detroit, May 12-14. Dr. Samuel X. Radbill, 7043 Elmwood Ave., Philadelphia 42, Secretary.

AMERICAN ASSOCIATION OF IMMUNOLOGISTS, San Francisco, April 10-16. Dr. F. S. Cheever, University of Pittsburgh School of Public Health, Pittsburgh 13, Secretary.

AMERICAN ASSOCIATION ON MENTAL DEFICIENCY, Statler Hotel, Detroit, May 24-28. Dr. Lloyd N. Yepsen, New Lisbon, N. J., Secretary.

AMERICAN ASSOCIATION OF PATHOLOGISTS AND BACTERIOLOGISTS, The Shamrock, Houston, Texas, April 7-9. Dr. Edward A. Gall, Cincinnati General Hospital, Cincinnati 29, Secretary.

AMERICAN ASSOCIATION OF RAILWAY SURGEONS, Drake Hotel, Chicago, April 12-14. Dr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Secretary.

AMERICAN ASSOCIATION FOR THE STUDY OF NEOPLASTIC DISEASES, Lord Baltimore Hotel, Baltimore, May 5-7. Dr. Bruce H. Sisler, P. O. Box 268, Gatlinburg, Tenn., Secretary.

AMERICAN ASSOCIATION FOR THORACIC SURGERY, Chalfonte-Haddon Hall, Atlantic City, N. J., April 24-26. Dr. Paul C. Samson, 3959 Happy Valley Rd., Lafayette, Calif., Secretary.

AMERICAN COLLEGE OF ALLERGISTS, Morrison Hotel, Chicago, April 25-30. Dr. Fred W. Wittich, 401 LaSalle Med. Bldg., Minneapolis 2, Secretary.

AMERICAN COLLEGE OF CARDIOLOGY, Hotel Biltmore, New York, May 19-21. Dr. Philip Reichert, 140 West 57th St., New York 19, Secretary.

AMERICAN COLLEGE OF PHYSICIANS, Benjamin Franklin and Bellevue-Stratford Hotels, Philadelphia, April 25-29. Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Executive Secretary.

AMERICAN DERMATOLOGICAL ASSOCIATION, Bellevue-Biltmore Hotel, Belleair, Fla., April 17-21. Dr. J. Lamar Callaway, Duke Hospital, Durham, N. C., Secretary.

AMERICAN FEDERATION FOR CLINICAL RESEARCH, Haddon Hall, Atlantic City, N. J., May 1. Dr. Lawrence E. Hinkle Jr., 525 East 68th St., New York 21, Secretary.

AMERICAN GERIATRICS SOCIETY, Hotel Roosevelt, New York, April 21-22. Dr. Malford W. Thewlis, 25 Mechanic St., Wakefield, R. I., Secretary.

AMERICAN GOITER ASSOCIATION, Skirvin Hotel, Oklahoma City, April 28-30. Dr. John C. McClintock, 149½ Washington Ave., Albany 10, N. Y., Secretary.

AMERICAN GYNECOLOGICAL SOCIETY, Chateau Frontenac, Quebec, Canada, May 23-25. Dr. John I. Brewer, 104 S. Michigan Blvd., Chicago 3, Secretary.

AMERICAN PHYSIOLOGICAL SOCIETY, San Francisco, April 11-16. Dr. W. F. Hamilton, Medical College of Georgia, Augusta, Ga., Secretary.

AMERICAN PSYCHIATRIC ASSOCIATION, Traymore and Claridge Hotels, Atlantic City, N. J., May 9-13. Dr. William Malamud, 80 East Concord St., Boston 18, Secretary.

AMERICAN PSYCHOSOMATIC SOCIETY, Claridge Hotel, Atlantic City, N. J., May 4-5. Dr. Theodore Lidz, 333 Cedar St., New Haven 11, Conn., Secretary.

AMERICAN RADIUM SOCIETY, Shoreham Hotel, Washington, D. C., April 21-23. Dr. Robert E. Fricke, 102 Second Ave. S.W., Rochester, Minn., Secretary.

AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, Palace Hotel, San Francisco, Apr. 10-15. Dr. Philip Handler, Duke University, Durham, N. C., Secretary.

AMERICAN SOCIETY FOR CLINICAL INVESTIGATION, Haddon Hall, Atlantic City, N. J., May 2. Dr. J. D. Meyers, 622 West 168th St., New York 32, Secretary.

AMERICAN SOCIETY FOR EXPERIMENTAL PATHOLOGY, San Francisco, April 10-16. Dr. Cyrus C. Erickson, 874 Union Avenue, Memphis 3, Tenn., Secretary.

AMERICAN SOCIETY OF MAXILLOFACIAL SURGEONS, Brown Hotel, Louisville, Ky., May 9-11. Dr. John A. Drummond, 1414 Drummond St., Montreal, Canada, Secretary

AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, San Francisco, April 10-16. Dr. Carl C. Pfeiffer, Emory University School of Medicine, Emory University, Ga., Secretary.

AMERICAN SURGICAL ASSOCIATION, The Warwick, Philadelphia, April 27-29. Dr. R. Kennedy Gilchrist, 59 East Madison St., Chicago 3, Secretary.

AMERICAN TRUDEAU SOCIETY, Schroeder Hotel, Milwaukee, May 23-27. Dr. W. G. Childress, 1790 Broadway, New York 19, Secretary.

AMERICAN UROLOGICAL ASSOCIATION, Hotel Biltmore, Los Angeles, May 16-19. Dr. Charles H. deT. Shivers, 121 South Illinois Ave., Atlantic City, N. J., Secretary.

AMERICAN VENEREAL DISEASE ASSOCIATION, Washington, D. C., Apr. 28-29. Dr. John C. Hume, 615 N. Wolfe St., Baltimore 5, Secretary.

ARIZONA MEDICAL ASSOCIATION, El Conquistador, Tucson, May 4-7. Dr. Dermont W. Melick, 401 Security Building, Phoenix, Secretary.

ASSOCIATION OF AMERICAN PHYSICIANS, Chalfonte-Haddon Hall, Atlantic City, N. J., May 3-4. Dr. W. Barry Wood Jr., 600 S. Kingshighway Blvd., St. Louis 10, Secretary.

CALIFORNIA MEDICAL ASSOCIATION, Palace Hotel, San Francisco, May 1-5. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

CATHOLIC HOSPITAL ASSOCIATION OF THE U. S. AND CANADA, Kiel Auditorium, St. Louis, May 16-19. Mr. M. R. Kneifl, 1438 South Grand Blvd., St. Louis 4, Executive Secretary.

CONFERENCE ON MICROCIRCULATORY PHYSIOLOGY AND PATHOLOGY, Benjamin Franklin Hotel, Philadelphia, April 5. Dr. George P. Fulton, Boston University College of Liberal Arts, 725 Commonwealth Ave., Boston 15, Chairman.

CONNECTICUT STATE MEDICAL SOCIETY, Stratfield Hotel, Bridgeport, April 26-28. Dr. Creighton Barker, 160 St. Ronan St., New Haven, Executive Secretary.

EASTERN STATES HEALTH EDUCATION CONFERENCE, New York Academy of Medicine, New York, April 21-22. Dr. Iago Galdston, 2 East 103rd St., New York 29, Secretary.

FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, San Francisco, April 11-15. Dr. M. O. Lee, 2101 Constitution Avenue, Washington, D. C., Secretary.

FLORIDA MEDICAL ASSOCIATION, Vinoy Park Hotel, St. Petersburg, April 3-6. Dr. Samuel M. Day, P. O. Box 1018, Jacksonville, Secretary.

GEORGIA, MEDICAL ASSOCIATION OF, Bon Air Hotel, Augusta, May 1-4. Mr. Milton D. Kreuger, 875 West Peachtree St., Atlanta, Executive Secretary.

HAWAII MEDICAL ASSOCIATION, Honolulu, May 5-8. Dr. Samuel L. Yee, 510 South Beretania St., Honolulu 13, Secretary.

ILLINOIS STATE MEDICAL SOCIETY, Hotel Sherman, Chicago, May 17-20. Dr. Harold M. Camp, 224 South Main St., Monmouth, Secretary.

INDUSTRIAL MEDICAL ASSOCIATION, Buffalo, N. Y., April 23-29. Dr. Glenn Gardiner, Inland Steel Co., East Chicago, Ind., Secretary.

IOWA STATE MEDICAL SOCIETY, Veterans' Memorial Auditorium, Des Moines, April 24-27. Dr. R. F. Birge, 529 36th St., Des Moines 12, Secretary.

JOHN A. ANDREW CLINICAL SOCIETY, Memorial Hospital, Tuskegee Institute, Ala., April 3-8. Dr. Eugene H. Dibble Jr., John A. Andrew Memorial Hospital, Tuskegee Institute, Alabama, Secretary.

KANSAS MEDICAL SOCIETY, Baker Hotel, Hutchinson, May 1-5. Dr. J. A. Butin, 315 West Fourth St., Topeka, Secretary.

LOUISIANA STATE MEDICAL SOCIETY, Roosevelt Hotel, New Orleans, May 2-4. Dr. C. Grenes Cole, 1430 Tulane Ave., New Orleans 12, Secretary.

MARYLAND, MEDICAL AND CHIRURGICAL FACULTY OF THE STATE OF, Baltimore, April 21-23. Dr. Everett S. Diggs, 1211 Cathedral St., Baltimore, Secretary.

MASSACHUSETTS MEDICAL SOCIETY, Hotel Statler, Boston, May 17-19. Dr. Robert W. Buck, 22 Fenway, Boston 15, Secretary.

MEDICAL LIBRARY ASSOCIATION, Hotel Schroeder, Milwaukee, May 17-20. Miss Esther Judkins, Rockefeller Institute, 66th St. at York Ave., New York 21, Secretary.

MID-CENTRAL STATES ORTHOPAEDIC SOCIETY, Sheraton Hotel and St. Louis Medical Society Auditorium, St. Louis, April 15-16. Dr. H. O. Anderson, 3244 East Douglas St., Wichita, Kans., Secretary.

MIDWEST REGIONAL CONFERENCE, AMERICAN PSYCHIATRIC ASSOCIATION, Nebraska Psychiatric Institute, Omaha, Apr. 22-23. Dr. Harold R. Martin, Nebraska Psychiatric Institute, Omaha, Chairman, Program Committee.

MINNESOTA STATE MEDICAL ASSOCIATION, Hotel Radisson, Minneapolis, May 23-25. Mr. R. R. Rosell, Lowry Medical Arts Bldg., St. Paul 2, Executive Secretary.

MISSISSIPPI STATE MEDICAL ASSOCIATION, Hotel Buena Vista, Biloxi, May 10-12. Mr. Rowland B. Kennedy, 860 Milner Bldg., Jackson, Executive Secretary.

NATIONAL GASTROINTESTINAL CANCER CONFERENCE, Hosack Hall, New York Academy of Medicine, New York, April 4-5. Dr. Morris K. Barrett, National Cancer Institute, Bethesda 14, Maryland, Executive Secretary.

NATIONAL TUBERCULOSIS ASSOCIATION, Hotel Schroeder, Milwaukee, May 23-27. Dr. James E. Perkins, 1790 Broadway, New York 19, Managing Director.

NEBRASKA STATE MEDICAL ASSOCIATION, Hotel Paxton, Omaha, May 16-19. Dr. R. B. Adams, 1315 Sharp Bldg., Lincoln, Secretary.

NEW JERSEY, MEDICAL SOCIETY OF, Ambassador Hotel, Atlantic City, April 17-20. Dr. Marcus H. Greifinger, 315 West State St., Trenton 8, Secretary.

NEW MEXICO MEDICAL SOCIETY, Hilton Hotel, Albuquerque, May 4-6. Mr. Ralph R. Marshall, 223 First National Bank Bldg., Albuquerque, Executive Secretary.

NEW YORK, MEDICAL SOCIETY OF THE STATE OF, Hotel Statler, Buffalo, May 9-13. Dr. Walter P. Anderton, 386 Fourth Avenue, New York 16, Secretary.

NORTH CAROLINA, MEDICAL SOCIETY OF THE STATE OF, Hotel Carolina, Pinehurst, May 2-4. Mr. James T. Barnes, 203 Capitol Club Building, Raleigh, Executive Secretary.

NORTH DAKOTA STATE MEDICAL ASSOCIATION, Hotel Prince, Bismarck, April 30-May 3. Dr. E. H. Boerth, Box 1198, Bismarck, Secretary.

OHIO STATE MEDICAL ASSOCIATION, Netherland-Plaza Hotel, Cincinnati, April 19-21. Mr. Charles S. Nelson, 79 E. State St., Columbus 15, Executive Secretary.

OKLAHOMA STATE MEDICAL ASSOCIATION, Mayo Hotel, Tulsa, May 8-11. Mr. R. H. Graham, 1227 Classen Drive, Oklahoma City, Executive Secretary.

PACIFIC NORTHWEST SOCIETY OF PLASTIC AND RECONSTRUCTIVE SURGEONS, Spokane, Wash., May 21. Dr. E. E. Banfield, Medical Arts Bldg., Tacoma 2, Washington, Secretary.

RHODE ISLAND MEDICAL SOCIETY, Rhode Island Medical Society Library, Providence, May 4-5. Dr. Thomas Perry Jr., 106 Francis St., Providence 3, Secretary.

ROCKY MOUNTAIN MEDICAL CONFERENCE, Hilton Hotel, Albuquerque, N. Mex., May 4-6. Mr. Ralph R. Marshall, 223-224 First National Bank, Albuquerque, N. Mex., Secretary.

SECTIONAL MEETINGS, AMERICAN COLLEGE OF SURGEONS:

IDAHO, Sun Valley, Sun Valley Lodge, April 18-20. Dr. James H. Hawley, 105 North 8th St., Boise, Chairman.

MANITOBA, Winnipeg, The Fort Garry, April 25-26. Dr. Paul H. T. Thorlakson, Winnipeg Clinic, Winnipeg, Manitoba, Chairman.

TENNESSEE, Nashville, Dinkler-Andrew Jackson Hotel and War Memorial Bldg., April 4-6. Dr. James A. Kirtley Jr., 104 Twentieth Ave. North, Nashville, Chairman.

SOCIETY OF AMERICAN BACTERIOLOGISTS, Statler Hotel, New York, May 8-13. Dr. John Hays Bailey, Sterling Winthrop Research Institute, Rensselaer, N. Y., Secretary.

SOUTH CAROLINA MEDICAL ASSOCIATION, Francis Marion Hotel, Charleston, May 10-12. Dr. Robert Wilson, 165 Rutledge Ave., Charleston, Secretary.

SOUTH DAKOTA STATE MEDICAL ASSOCIATION, Lawler Hotel, Mitchell, May 21-24. Dr. G. I. W. Cottam, 300 First National Bank Bldg., Sioux Falls, Secretary.

SOUTHERN BRANCH, AMERICAN PUBLIC HEALTH ASSOCIATION, New Orleans, May 11-13. Dr. Frank M. Hall, P. O. Box 491, Gainesville, Fla., Secretary.

STUDENT AMERICAN MEDICAL ASSOCIATION, Sherman Hotel, Chicago, May 6-8. Mr. Russell F. Staudacher, 510 N. Dearborn St., Chicago 10, Executive Secretary.

TENNESSEE STATE MEDICAL ASSOCIATION, Read House, Chattanooga, April 10-13. Dr. R. H. Kampmeier, 706 Church St., Nashville 3, Secretary.

TEXAS MEDICAL ASSOCIATION, Texas Hotel, Fort Worth, April 24-27. Dr. J. M. Travis Sr., 1801 North Lamar Blvd., Austin, Secretary.

UNITED STATES-MEXICO BORDER PUBLIC HEALTH ASSOCIATION, Hotel del Bosque, Mexico, D. F., May 6-9. Dr. Sidney B. Clark, 204 U. S. Court, El Paso, Texas, Secretary.

WESTERN BRANCH, AMERICAN PUBLIC HEALTH ASSOCIATION, Phoenix, Ariz., April 19-22. Mrs. L. Amy Darter, Division of Laboratories, State Dept. of Public Health, Berkeley, Calif., Secretary.

WESTERN INDUSTRIAL MEDICAL ASSOCIATION, Sir Francis Drake Hotel, San Francisco, April 30. Dr. Edward J. Zaik, 740 S. Olive St., Room 320, Los Angeles 14, Secretary.

WISCONSIN, STATE MEDICAL SOCIETY OF, Hotel Schroeder, Milwaukee, May 3-5. Mr. Charles H. Crownhart, 704 East Gorham St., Madison 3, Secretary.

FOREIGN AND INTERNATIONAL

ASSOCIATION OF SURGEONS OF GREAT BRITAIN AND IRELAND, University of Glasgow, Glasgow, Scotland, April 14-16. Dr. Henry W. S. Wright, 45 Lincoln's Inn Fields, London W.C.2, England, Hon. Secretary.

AUSTRALASIAN MEDICAL CONGRESS, Sydney, N.S.W., Australia, Aug. 20-27. For information write: Federal Council of the B.M.A. in Australia, 135 Macquaire St., Syndey, N.S.W., Australia.

BRITISH MEDICAL ASSOCIATION, Representative Meeting, London, England, June 1-4. Dr. A. Macrae, B.M.A. House, Tavistock Square, London, W.C.1, England, Secretary.

CANADIAN AND BRITISH MEDICAL ASSOCIATIONS, Joint Meeting, Toronto, Canada, June 20-22. Dr. Arthur D. Kelly, 244 St. George St., Toronto, Canada, General Secretary.

COMMONWEALTH HEALTH AND TUBERCULOSIS CONFERENCE, Royal Festival Hall, London, England, June 21-25. Mr. J. H. Harley Williams, Tavistock House North, Tavistock Square, London, W.C.1, England, Secretary General.

CONGRESS OF INTERNATIONAL ASSOCIATION OF APPLIED PSYCHOLOGY, London, England, July 18-23. Dr. C. B. Frisby, National Institute of Industrial Psychology, 14 Welbeck St., London, W.1, England, President.

CONGRESS OF INTERNATIONAL ASSOCIATION OF PSYCHOTECHNOLOGY, London, England, July 18-23. For information write: Dr. C. B. Frisby, Director, National Institute of Industrial Psychology, 14 Welbeck St., London, W.1, England.

CONGRESS OF THE INTERNATIONAL ASSOCIATION FOR THE STUDY OF THE BRONCHI, Stockholm, Sweden, June 18-19. For information write: Dr. J. M. Lemoine, 187 boulevard St. Germain, Paris 7e, France.

CONGRESS OF INTERNATIONAL DIABETES FEDERATION, Cambridge, England, July 4-8. Mr. James G. L. Jackson, 152 Harley St., London, W.1, England, Executive Secretary General.

CONGRESS OF INTERNATIONAL SOCIETY OF SURGERY, Copenhagen, Denmark, July 23-29. Dr. L. Dejardin, 141 rue Belliard, Brussels, Belgium, General Secretary.

EUROPEAN CONGRESS ON RHEUMATISM, Scheveningen, The Hague, Netherlands, June 13-17. Dr. H. van Swaay, Pieter Bothstraat 12, The Hague, Netherlands, Secretary.

HEALTH CONGRESS OF THE ROYAL SANITARY INSTITUTE, Bournemouth, England, April 26-29. Mr. P. Arthur Wells, Royal Sanitary Institute, 90 Buckingham Palace Road, London, S.W.1, England, Secretary.

HISPANO-PORTUGUESE CONGRESS OF OBSTETRICS AND GYNECOLOGY, Seville, Spain, April 13-16. Dr. M. Recasens, Calle Munoz Olive 7, Seville, Spain, General Secretary.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Shoreham Hotel, Washington, D. C., U. S. A., April 24-29. Dr. Eugene P. Pendergrass, 3400 Spruce St., Philadelphia 4, Pa., U. S. A., Secretary General.

INTERNATIONAL ANATOMICAL CONGRESS, Paris, France, July 25-30. Prof. Gaston Cordier, 45, rue des Saints-Pères, Paris 6e, France, Secretary General.

INTERNATIONAL CONGRESS OF ALLERGOLOGY, Rio de Janeiro, Brazil, S. A., Nov. 6-13. Dr. Bernard N. Halpern, 197 boulevard St. Germain, Paris 7e, France, Secretary General.

INTERNATIONAL CONGRESS OF ANGIOLOGY AND HISTOPATHOLOGY, Fribourg, Switzerland, Sept. 2-5. For information write: Dr. Gerson, 4 rue Pasquier, Paris 8e, France.

INTERNATIONAL CONGRESS OF BIOCHEMISTRY, Brussels, Belgium, Aug. 1-6. Prof. C. Liebecq, 17 Place Delcour, Liège, Belgium, Secretary General.

INTERNATIONAL CONGRESS OF COMPARATIVE PATHOLOGY, Lausanne, Switzerland, May 26-31. Professor Hauduroy, 19 rue Cesar Roux, Lausanne, Switzerland, Secretary General.

INTERNATIONAL CONGRESS OF CRIMINOLOGY, London, England, Sept. 11-18. For information write: Dr. Carroll, 28 Weymouth St., London, W.1, England.

INTERNATIONAL CONGRESS OF EUROPEAN SOCIETY OF HAEMATOLOGY, Freiburg i,Br., Germany, Sept. 20-24. Prof. Dr. L. Heilmeyer, Hugstetter Strasse 55, Freiburg i,Br., Germany, Chairman.

INTERNATIONAL CONGRESS OF LIBRARIANSHIP AND DOCUMENTATION, Brussels, Belgium, Sept. 11-18. For information write: Dr. A. C. Breycha-Vauthier, Librarian, United Nations, Geneva, Switzerland.

INTERNATIONAL CONGRESS OF NEUROPATHOLOGY, London, England, Sept. 12-17. Dr. W. H. McMenemey, Maida Vale Hospital for Nervous Diseases, London, W.9, England, Secretary.

INTERNATIONAL CONGRESS OF PLASTIC SURGERY, Stockholm, Sweden, Aug. 1-4, and Uppsala, Sweden, Aug. 5. Dr. Tord Skoog, Uppsala, Sweden, General Secretary.

INTERNATIONAL CONGRESS ON URINARY LITHIASIS, Evian, France, Sept. 2-4. Mr. Rossollin-Grandville, Direction Cachet, Evian (Hte-Savoie), France, Secretary General.

INTERNATIONAL CONGRESS OF UROLOGY, Athens, Greece, April 10-18. Dr. Z. Kaires, 25, rue Voukourestion, Athens, Greece, Secretary General.

INTERNATIONAL HOSPITAL CONGRESS, Lucerne, Switzerland, May 29-June 3. Capt. J. E. Stone, International Hospital Federation, 10 Old Jewry, London, E.C.2, England, Hon. Secretary.

INTERNATIONAL MEDICAL CONGRESS, Verona, Italy, Sept. 1-4. For information write: c/o Offices of the International Verona Fair, Piazza Bra., Verona, Italy.

INTERNATIONAL SOCIETY FOR THE STUDY OF BIOLOGICAL RHYTHMS, Stockholm, Sweden, Sept. 15-17. For information write: Prof. Ture Petrén, Karolinska Institutet, Stockholm 60, Sweden.

INTERNATIONAL SURGICAL CONGRESS, Geneva, Switzerland, May 23-26. Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Illinois, U. S. A., Secretary General.

INTERNATIONAL SYNDICATE OF GYNECOLOGISTS AND OBSTETRICIANS, Meeting Hall of Medical Societies, Paris, France, June 27-28. Dr. Jacques Courtois, 1, rue Racine, Saint-Germain-en-Laye (S & O), France, Secretary General.

IRISH OPHTHALMOLOGICAL SOCIETY, Dublin, Ireland, May 12-14.

MIDDLE EAST MEDICAL ASSEMBLY, Campus of American University of Beirut, Beirut, Lebanon April 22-24. Dr. John L. Wilson, American University of Beirut, Beirut, Lebanon, Chairman.

NEURORADIOLOGIC SYMPOSIUM, London, England, Sept. 13-17. Dr. R. D. Hoare, National Hospital, Queen Square, London, W.C.1, England, Secretary.

PAN AMERICAN CONGRESS OF OPHTHALMOLOGY, Santiago, Chile, S. A., Jan. 9-14, 1956. Dr. Rene Contardo, Huerfanos 930, Of. 74, Santiago, Chile, Secretary General.

PAN AMERICAN CONGRESS ON RHEUMATIC DISEASES, Rio de Janeiro and Sao Paulo, Brazil, S. A., Aug. 14-20. For information write: Dr. Waldemar Bianchi, 126 Avenida Franklin D. Roosevelt, Rio de Janeiro, Brazil, S. A.

VENEZUELAN CONGRESS OF MEDICAL SCIENCES, Caracas, Venezuela, S. A., Nov. 18-26. Dr. A. L. Briceno Rossi, Apartado 4412, Ofic. del Este, Caracas, Venezuela, S. A., Secretary General.

WORLD CONGRESS OF ANESTHESIOLOGISTS, Scheveningen, Netherlands, Sept. 5-10. For information write: Mr. W. A. Fentener van Vlissingen, Noord-Houdringelaan, 24, Bilthoven, Netherlands.

WORLD FEDERATION FOR MENTAL HEALTH, Istanbul, Turkey, Aug. 21. For information write: Miss E. M. Thornton, 19 Manchester St., London, W.1, England.

WORLD MEDICAL ASSOCIATION, Vienna, Austria, Sept. 20-26. Dr. Louis H. Bauer, 345 East 46th St., New York 17, N. Y., U. S. A., Secretary General.

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 21-23. Sec., Dr. D. G. Gill, 537 Dexter Ave., Montgomery 4.

ARIZONA:* *Examination and Reciprocity.* Phoenix, April 13-15. Ex. Sec., Mr. Robert Carpenter, 401 Security Bldg., Phoenix.

ARKANSAS:* *Examination.* Little Rock, June 9-10. Sec., Dr. Joe Verser, Harrisburg.

CALIFORNIA: *Written.* San Francisco, June 20-23; Los Angeles, Aug. 22-25; and Sacramento, Oct. 17-20. *Oral and Clinical Examinations for Foreign Medical School Graduates.* San Francisco, June 19; Los Angeles, Aug. 21; and San Francisco, Nov. 13. *Oral Examination for Reciprocity Applications.* San Francisco, June 18; Los Angeles, Aug. 20; and San Francisco, Nov. 12. Sec., Dr. Louis E. Jones, Room 536, 1020 N Street, Sacramento.

COLORADO:* *Examination.* Denver, June 14-15. Final date for filing applications is May 13. *Reciprocity.* Denver, April 12. Final date for filing applications was March 14. Exec. Sec., Miss Beulah H. Hudgens, 831 Republic Bldg., Denver 2.

DELAWARE: *Examination.* Dover, July 12-14. *Endorsement.* Dover, July 21. Final date for filing applications is June 15. Sec., Dr. Joseph S. McDaniel, Dover.

DISTRICT OF COLUMBIA:* *Examination.* Washington, May 9-10. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Avenue, N.W., Washington.

FLORIDA:* *Examination.* Jacksonville, June 26-28. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami.

GEORIGA: *Examination.* Atlanta and Augusta, June 7-8. *Reciprocity.* June 9. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta.

INDIANA: *Examination.* Indianapolis, June 21-23. Exec. Sec., Miss Ruth V. Kirk, 538 K. of P. Building, Indianapolis.

IOWA:* *Examination.* Iowa City, June 13-15. Exec. Sec., Mr. Ronald V. Saf, State Office Bldg., Des Moines.

KANSAS: *Examination and Endorsement.* Kansas City, June 8-9. Sec., Dr. O. M. Davidson, 872 New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination.* Louisville, June 6-8. Asst. Sec., Mr. Raymond F. Dixon, 620 S. 3rd St., Louisville.

LOUISIANA: *Homeopathic. Examination and Reciprocity.* Subject to Call. Sec., Dr. F. H. Hardenstein, 903 Pere Marquette Bldg., New Orleans 12.

MARYLAND: *Regular Examination.* Baltimore, June 21-24. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore 18. *Homeopathic. Reciprocity.* Washington, D. C., April 12. *Examination. Written.* Baltimore, June 20-22. Sec., Dr. Robert H. Reddick, Eastern Shore State Hospital, Cambridge.

MASSACHUSETTS: *Examination.* Boston, July 12-15. Sec., Dr. Robert C. Cochrane, Room 37, State House, Boston.

MICHIGAN:* *Examination.* Ann Arbor and Detroit, June 15-17 (tentative). Sec., Dr. J. Earl McIntyre, 118 Stevens T. Mason Bldg., Lansing 8.

MINNESOTA:* *Examination.* Minneapolis, April 19-21 and June 14-16. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: *Examination and Reciprocity.* Jackson, June 27-29. Asst. Sec., Dr. R. N. Whitfield, State Board of Health, Jackson.

MONTANA: *Examination and Reciprocity.* Helena, April 4-6. Sec., Dr. S. A. Cooney, 214 Power Block, Helena.

NEBRASKA:* *Examination.* Omaha, June. Director, Bureau of Examining Boards, Mr. Husted K. Watson, State Capitol Bldg., Room 1009, Lincoln 9.

NEVADA:* *Examination and Reciprocity.* Reno, April 5. Sec., Dr. G. H. Ross, 112 N. Curry St., Carson City.

NEW MEXICO:* *Examination and Reciprocity.* Santa Fe, Apr. 11-12. Sec., Dr. R. C. Derbyshire, 227 E. Palace Ave., Santa Fe.

NORTH CAROLINA: *Examination.* Raleigh, June 20-23. *Reciprocity.* Pinehurst, May 2. Sec., Dr. Joseph J. Combs, 716 Professional Building, Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, July 6-8. *Reciprocity.* Grand Forks, July 9. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Reciprocity.* Columbus, April 5. *Written.* Columbus, June 13-15. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

OKLAHOMA:* *Examination.* Oklahoma City, June 7-8. Sec., Dr. C. Gallagher, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Examination.* Portland, July. *Reciprocity.* Portland, April 7-9. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland 4.

PENNSYLVANIA: *Examination.* Philadelphia and Pittsburgh, July. Acting Sec., Mrs. Marguerite G. Steiner, Box 911, Harrisburg.

RHODE ISLAND:* *Examination.* Providence, April 7-8. Administrator of Professional Regulation, Mr. Thomas B. Casey, Room 366, State Office Bldg., Providence.

SOUTH CAROLINA: *Examination.* Columbia, June 27-29. *Reciprocity.* Charleston, May 10. Sec., Mr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA:* *Examination and Reciprocity.* Rapid City, July 19-20. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

TEXAS:* *Examination and Reciprocity.* Fort Worth, June 20-22. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

VIRGINIA: *Examination.* Richmond, June 16-18. *Reciprocity.* Richmond, June 15. Address: The Secretary, 631 First St., S.W., Roanoke.

WASHINGTON:* *Examination and Reciprocity.* Seattle, July 10-13. Sec., Mr. Edward C. Dohm, Capitol Bldg., Olympia.

WEST VIRGINIA: *Reciprocity.* Charleston, April 4. Sec., Dr. N. H. Dyer, State Office Bldg., No. 3, Charleston 5.

WISCONSIN:* *Reciprocity.* Madison, April 14-16. The board will also interview applicants for Temporary Educational Permits who have commenced their training previous to the meeting. Sec., Dr. Thomas W. Tormey, Room 1140, State Office Bldg., Madison 2.

WYOMING: *Examination and Reciprocity.* Cheyenne, June 6. Sec., Dr Franklin D. Yoder, State Office Bldg., Cheyenne.

ALASKA:* On application. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Sec., Dr. John E. Kennedy, Agana.

HAWAII: *Examination.* Honolulu, July 11-14. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

VIRGIN ISLANDS: *Examination and Reciprocity.* St. Thomas, June 8-9. Sec., Dr. Earle M. Rice, St. Thomas.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: *Reciprocity.* Phoenix, April 16. Sec., Dr. M. R. Richter, 2910 N. 7th Ave., Phoenix.

ARKANSAS: *Examination.* Little Rock, May 3-4. Sec., Mr. S. C. Dellinger, Zoology Dept., University of Arkansas, Fayetteville.

DISTRICT OF COLUMBIA: *Examination.* Washington, April 18-19. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., N.W., Washington.

FLORIDA: *Examination.* Miami and Gainesville, May 14. Sec., Mr. M. W. Emmel, Box 340, University of Florida, Gainesville.

IOWA: *Examination.* Des Moines, April 12. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.

MINNESOTA: *Examination.* Minneapolis, April 5-6. Sec., Dr. Raymond N. Bieter, 126 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: *Examination.* Omaha, May 3-4. Director, Mr. Husted K. Watson, 1009 State Capitol, Lincoln.

NEVADA: *Examination.* Reno, April 5. Sec., Dr. Donald G. Cooney, Box 9002, University Station, Reno.

OKLAHOMA: Oklahoma City, April 7-8. Sec., Dr. C. Gallagher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, June 4, Sept. 10, and Dec. 3. Sec., Mr. Charles D. Byrne, State Board of Higher Education, Eugene.

SOUTH DAKOTA: *Examination.* Vermillion, June 10-11. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

TEXAS: *Examination.* Galveston, Houston and Dallas, April 15-16. Chief Clerk, Mrs. Betty Ratcliff, 407 Perry-Brooks Bldg., Austin.

WASHINGTON: *Examination.* Seattle, July 6-7. Sec., Mr. Edward C. Dohm, Capitol Bldg., Olympia.

WISCONSIN: *Examination.* Milwaukee, May 14. Sec., Mr. William H. Barger, 621 Ransom St., Ripon.

ALASKA: On application. Juneau or other towns in Territory as decided by Board. *Reciprocity.* On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

*Basic Science Certificate required.

MAGAZINE–TELEVISION REPORT

The following list of current medical articles in mass-circulation magazines and forthcoming network television programs on medical subjects is published each week only for the information of readers of THE JOURNAL. *Unless specifically stated, the American Medical Association neither approves nor disapproves of the articles and programs reported.*

TELEVISION

Tuesday, April 5

ABC-TV, 7:30 p. m. EST. "Cavalcade of America." The story of Nurse Clara Maas who participated in a yellow fever experiment in Cuba and died as a result of the bite of a Stegomyia mosquito; entitled, "No Greater Love."

MAGAZINES

Life, March 21, 1955

"Science Tackles Radiation Peril"

"The mysterious effects of radiation on man and his descendants are now being investigated by scientists in some 240 U. S. laboratories." The pictures and the story describe experimentation with irradiated animals, effects of radiation on the human body, and its consequent destruction of chromosomes and chemical changes in the structure of genes.

"A Legacy to Mankind"

A photographic portrait and tribute to Dr. Alexander Fleming, who died last month at the age of 73. "His death was mourned around the world. But the fungoid progeny of his find live on, to do incalculable good to generations of men as yet unborn."

The Saturday Evening Post, March 26, 1955

"Patients on Parole," by Ruth and Edward Brecher

Maryland's plan of 300 "careholders" cooperating in its state-wide program for rehabilitating mental patients by placing them in selected foster homes has provided a solution for "recovered" patients who have no place to go. Foster homes frequently bring results better than mental hospital therapy achieves.

Parade, April 3, 1955

"What Makes People Cough?" by Robert P. Goldman

A description of the cough, "that remarkable little body explosion," and how the nervous system and muscles cooperate to cause it. The writer tells of several drugs that physicians prescribe to relieve coughing and its causes.

American Weekly, April 3, 1955

"Woman's Marvelous Cycle of Life," by William Engle

Physicians can now prescribe a variety of drugs to relieve the discomfort of menstruation. The article also answers several questions concerning exercise, regularity of cycle, bathing, and hormones in relation to the occurrence of the menstrual period.

Woman's Day, April, 1955

"The Man Who Is Whipping Polio," by Dr. Delos Smith

This article is a personal profile of Dr. Jonas E. Salk and his work in developing an effective poliomyelitis vaccine. Its publication this month is keyed to the forthcoming announcement of the results of last year's mass inoculations.

Woman's Home Companion, April, 1955

"When Baby Is Hurt!" by Mary Scott Welch

Advice to the young mother in treating her infant for minor burns, cuts, bumps, and other minor accidents. The mother is urged to call the doctor if serious symptoms occur.

Town Journal, April, 1955

"Pain—Life-Saver in Disguise," by Ruth and Edward Brecher

This article explains how nerves alert the brain to injuries sustained in various parts of the body and "is a sort of speedometer which measures the speed with which tissue damage is occurring." Researchers classify pain in three categories: pricking, burning, and aching. The article also discusses individual sensitivity and varying reactions of sufferers.

(A condensation of this article appears in the April issue of the *Reader's Digest* and was reviewed in the March 26 issue of THE JOURNAL.)

DEATHS

Hook, Frederick Raymond ⊕ Rear Admiral, U. S. Navy, retired, San Francisco; born in Rossville, Kan., March 19, 1889; University Medical College of Kansas City, Mo., 1913; subsequently interned at the Kansas City Hospital and at Kingston Hospital in Brooklyn; appointed an assistant surgeon in the U. S. Navy in 1917; promoted to captain, medical corps, U. S. Navy in 1941; advanced by reason of his combat decorations to the rank of rear admiral when placed on the retired list of officers of the Navy in May, 1948; completed several postgraduate courses in general surgery at Mayo Foundation, Rochester, Minn., and a course in orthopedic surgery at Harvard University, Cambridge, Mass.; served during World War I; awarded the Navy Cross for extraordinary heroism during the attack on Bois de Belleau in caring for the wounded under fire and at Blanc Mont for the establishment and maintenance of advanced dressing stations directly behind the front lines, the Army Distinguished Service Cross for establishing an advanced dressing station in an exposed position under heavy artillery and machine gun fire during an action near St. Etienne, France, the Army Silver Star Medal for action at Blanc Mont in October, 1918, and an Oak Leaf Cluster in lieu of a second Silver Star medal, for action on Bouresches on June 6, 1918; commanded the Naval hospitals at Chelsea, Mass., and at San Diego and Oakland, Calif.; awarded the Legion of Merit for "exceptionally meritorious conduct, as Force Medical Officer on the Staff of Commander South Pacific Area and Force from Nov. 30, 1942, to Feb. 19, 1945"; specialist certified by the American Board of Surgery; member of the American Surgical Association and the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; served as medical director of the Cancer Commission of the California Medical Association; well known in Washington, D. C., area, where he served as an instructor at the Naval Medical School from 1939 to 1942, as chief of surgery at the Naval hospitals in Washington, D. C., and Bethesda, Md., and in the Professional Division, Bureau of Medicine and Surgery, Navy Department; died in the Naval Hospital, San Diego, Feb. 2, aged 65, of hypertensive cardiovascular disease.

Seaman, Benjamin White ⊕ Hempstead, N. Y.; born in Rockville Center, Nov. 24, 1884; Cornell University Medical College, New York, 1907; past president of the Nassau County Medical Society and the Nassau County Surgical Society; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; on June 27, 1938, at a dinner attended by 450 citizens of Nassau County, was honored for his activities in connection with the establishment of the Meadowbrook Hospital; was the first person to receive the annual award, a medallion and citation, established by the *Nassau Daily Review-Star* for the "most valuable service to the whole community by a local resident"; served during World War I; formerly associated with the North Country Hospital in Glen Cove, Meadowbrook Hospital, and the Southside Hospital in Bay Shore; served as chief of the surgical division of the Nassau Hospital in Mineola, where he died Feb. 11, aged 70, of pulmonary embolism as the result of a fractured hip.

Brown, Henry Paul Jr. ⊕ Philadelphia; born in Philadelphia in 1888; University of Pennsylvania School of Medicine, Philadelphia, 1912; formerly on the faculty of the Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania; member of the founders' group of the American Board of Surgery; served during World War I; in World War II served in the South Pacific as head of an evacuation unit; an associate member of the American Medical Association; member of the American Surgical Association and Eastern Surgical Society; fellow of the American College of Surgeons; past president of the Aid Association of the Philadelphia County Medical Society; associated with the Pennsylvania and Presbyterian hospitals; consultant at the Children's Hospital; at one time medical missionary in China; died in the Hospital of the University of Pennsylvania Feb. 19, aged 67, of malignant lymphoma.

⊕ Indicates Member of the American Medical Association.

Knapp, Harold Jennings ⊕ Cleveland; born in Elyria, Ohio, July 15, 1887; Western Reserve University School of Medicine, Cleveland, 1919; specialist certified by the American Board of Public Health; life fellow of the American Public Health Association; for many years city health commissioner; formerly city chemist, director of all city laboratories, and chief of food and drug administration; director of the Diabetes Association of Greater Cleveland; member of the Welfare Federation's Health Council and committee on the chronically ill; member of the board of the Cleveland Health Museum and University Public Health Nursing District; served on the board of the Council and League of Nursing, Cleveland Hearing and Speech Center, Cleveland Hospital Council, and the American Red Cross; died Jan. 25, aged 67, of acute coronary thrombosis.

Mitchell, Edward Clay ⊕ Memphis, Tenn.; born Aug. 24, 1882; Northwestern University Medical School, Chicago, 1907; professor emeritus of pediatrics at the University of Tennessee College of Medicine; specialist certified by the American Board of Pediatrics; chairman, section on pediatrics, American Medical Association, 1938-1939; charter member and past president of the American Academy of Pediatrics; first president of both the Memphis and the Tennessee pediatric societies; past president of the old Central States Pediatric Society; served in France as colonel in the U. S. Army during World War I; at one time a member of the state public health council; associated with the John Gaston Hospital and the Baptist Memorial Hospital, where he died Feb. 1, aged 72, of heart disease.

Garland, James Gillis ⊕ Milwaukee; born in Antigo, Wis., Aug. 12, 1907; Marquette University School of Medicine, Milwaukee, 1932; associate clinical professor of surgery at his alma mater; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; immediate past president of the Medical Society of Milwaukee County; formerly treasurer of the Wisconsin Academy of Surgery; served during World War II; editor of *Milwaukee Medical Times;* on the staffs of St. Mary's Hospital, Evangelical Deaconess Hospital, Milwaukee County Hospital, and St. Luke's Hospital, where he died Jan. 25, aged 47, of arteriosclerotic heart disease with acute myocardial infarction.

Ferguson, Paul Stewart ⊕ Lieutenant (j. g.) U. S. Navy, retired, Knoxville, Tenn.; born in Richmond, Va., Nov. 23, 1899; Washington University School of Medicine, St. Louis, 1926; appointed a lieutenant (j. g.) medical corps of the U. S. Navy in June, 1926; retired for physical disability in 1929; served at the Naval Hospital, San Diego, Calif., and in the U. S. S. Canopus and Palos on the Asiatic Station; member of the College of American Pathologists; formerly assistant director of the staff in charge of hospital activities, American College of Surgeons; on the staff of the Knoxville General Hospital, where he died Dec. 28, 1954, aged 55, of adenocarcinoma of the prostate.

Gile, John Fowler, Hanover, N. H.; born in Tewksbury, Mass., July 5, 1893; Harvard Medical School, Boston, 1920; member of the founders' group of the American Board of Surgery; professor of clinical surgery emeritus at Dartmouth Medical School, where he was named life trustee in 1937; member of the Eastern Surgical Society, American Association for the Surgery of Trauma, and New England Surgical Society, of which he was formerly secretary; fellow of the American College of Surgeons; at one time vice-president of the New Hampshire Medical Society; on the staff of the Mary Hitchcock Memorial Hospital, where he died Jan. 29, aged 61, of coronary heart disease.

Anderson, Warren Bradley ⊕ Jackson, Mich.; Detroit Homeopathic College, 1912; died Feb. 18, aged 70, of heart failure.

Bailey, William Henry ⊕ Perryville, Mo.; Chicago Homeopathic Medical College, 1902; on the staff of the Perry County Memorial Hospital; for three years chairman of the library board; died Jan. 10, aged 80, of coronary occlusion.

Ballard, Carl Hardin ✠ Santa Monica, Calif.; University of Michigan Medical School, Ann Arbor, 1900; at one time practiced in Omaha, Neb., where he was on the faculty of the University of Nebraska College of Medicine; died Jan. 14, aged 77, of coronary thrombosis and generalized arteriosclerosis.

Breit, Hugo ✠ Binghamton, N. Y.; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany, 1926; on the staff of the Wilson Memorial Hospital in Johnson City, where he died Feb. 5, aged 55, of a heart attack.

Brumley, Stanford James ✠ Barker, N. Y.; University of Buffalo School of Medicine, 1935; served during World War II; past president of the Lockport Academy of Medicine; member of the county board of health; central school physician; on the staff of the Lockport (N. Y.) City Hospital; died Jan. 17, aged 43, of coronary thrombosis.

Butters, Charles Morgan ✠ Cambridge, Mass.; Tufts College Medical School, Boston, 1937; on the staff of the Somerville (Mass.) Hospital; accidentally drowned in Fort Lauderdale, Fla., Feb. 1, aged 52.

Cargill, Chauncey W. ✠ Mason City, Ill.; College of Physicians and Surgeons of Chicago, 1889; served as district health superintendent; died Feb. 20, aged 89, of heart disease.

Chappel, Halbert William, Hermosa Beach, Calif.; Cornell University Medical College, New York City, 1910; emeritus professor of orthopedics at the College of Medical Evangelists, Loma Linda and Los Angeles; for many years associated with the Garfield Hospital in Monterey Park, Children's Hospital, Los Angeles County General Hospital, the Hospital of the Good Samaritan in Los Angeles, and the Torrance (Calif.) Memorial Hospital, where he died Feb. 3, aged 76, of diabetes mellitus.

Chatel, Arthur Narcisse, Detroit; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1912; member of the Michigan State Medical Society; formerly on the staff of the East Side General Hospital and St. Joseph Mercy Hospital; died Feb. 15, aged 65, of chronic congestive heart failure and hypertensive heart disease.

Christian, David Alexander, III, Appomattox, Va.; University of Virginia Department of Medicine, Charlottesville, 1947; interned at the Baylor University Hospital in Dallas, Texas; served in the U. S. Naval Reserve; was shot and killed Feb. 26, aged 31.

Cohen, Mandel A. Isaac ✠ Chicago; Chicago College of Medicine and Surgery, 1916; served during World War I; died Feb. 27, aged 60.

Cole, I. Vincent, Seattle; Bennett College of Eclectic Medicine and Surgery, Chicago, 1893; died in Virginia Mason Hospital Feb. 13, aged 86, of acute left ventricular failure and diabetes mellitus.

Conrad, Agnes Mary Eigholz, Olema, Calif.; Columbus Medical College, 1886; died in the Franklin Hospital, San Francisco, Feb. 6, aged 87, of coronary thrombosis.

Cook, Malcolm MacDonnell ✠ Los Alamos, N. M.; Emory University (Ga.) School of Medicine, 1933; president of the Los Alamos County Medical Society; died Feb. 20, aged 48.

Cornell, John Webster, Chicago; the Hahnemann Medical College and Hospital, Chicago, 1900; formerly on the faculty of his alma mater; died Feb. 12, aged 79.

Cotton, Tolman W. ✠ Van Buren, Mo.; Beaumont Hospital Medical College, St. Louis, 1893; Barnes Medical College, St. Louis, 1899; past president of the Missouri State Medical Association; county health officer; died Feb. 6, aged 86, of heart disease.

Curtin, William Edward ✠ Plymouth, Mass.; Baltimore Medical College, 1913; formerly town health officer in Plymouth; for many years medical examiner of the Third Plymouth District and a member of the school committee; past surgeon of the Plymouth fire and police departments; medical director of the Cordage Company and physician to the county house of correction; past president of the Plymouth County Health Association; served on the staff of the Jordan Hospital, where he was past president; died Feb. 3, aged 66.

Denny, Alden Ray ✠ Griggsville, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1901; died Feb. 19, aged 80.

Dorais, Louis Pierre, San Francisco; College of Physicians and Surgeons of San Francisco, 1901; died Feb. 8, aged 90, of cerebral thrombosis.

Enders, William Henry ✠ Jackson, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; died in St. Joseph's Mercy Hospital, Ann Arbor, Feb. 21, aged 76, of carcinoma of the prostate with metastasis and uremia.

Erway, Charles Hendry, Elmira, N. Y.; Syracuse (N. Y.) University College of Medicine, 1905; member of the Industrial Medical Association and the Medical Society of the State of New York; village health officer at Elmira Heights for many years; at various times volunteer fireman, a member of the village board, school physician, and first coach of the Thomas A. Edison High School baseball team; medical director of the Eclipse Machine Division plant; died in the Arnot-Ogden Hospital Feb. 5, aged 75.

Fernhoff, William ✠ Woodridge, N. Y.; Medizinische Fakultät der Universität, Vienna, Austria, 1923; president of the Sullivan County Medical Society; coroner; fellow of the New York Academy of Medicine; member of the American Public Health Association; health officer; director of the Sullivan County Health Association; attending physician at Monticello (N. Y.) Hospital and the Maimonides Hospital in Liberty; died in the Cornwall (N. Y.) Hospital Jan. 31, aged 58, of injuries received when his automobile was struck by a truck.

Fleming, Aloysius Stephen ✠ Madison, N. J.; Minneapolis College of Physicians and Surgeons, 1897; died Jan. 19, aged 82, of cardiac failure, arteriosclerosis, and prostatic carcinoma.

Foote, Sherman Knevals ✠ Wyckoff, N. J.; Columbia University College of Physicians and Surgeons, New York, 1899; health officer of many towns; school physician for Wyckoff and Midland Park; formerly associated with the Roosevelt Hospital in New York; died in the Valley Hospital, Ridgewood, Feb. 12, aged 81, of carcinoma of the stomach.

Freeland, Clarence Furman ✠ Glendora, Miss.; Vanderbilt University School of Medicine, Nashville, Tenn., 1909; died in Greenwood-Leflore Hospital, Greenwood, Feb. 1, aged 71.

Furbush, Leroy Cleveland, Saugus, Mass.; Middlesex College of Medicine and Surgery, Cambridge, 1916; member of the Massachusetts Medical Society; member of the board of health; served as school physician; associated with the Union and Lynn hospitals in Lynn and the Melrose (Mass.) Hospital, where he died Feb. 15, aged 66, of coronary disease.

Furnas, Earl Emerson, Englewood, Ohio; Starling-Ohio Medical College, 1910; served during World War I; died in Tucson, Ariz., Feb. 1, aged 74, of myocardial infarction and hypertensive cardiovascular disease.

Gaines, Marion Toulmin ✠ Mobile, Ala.; Medical College of Alabama, Mobile, 1890; past president of the Medical Association of the State of Alabama and the Mobile County Medical Society; member of the American Academy of Dermatology and Syphilology; for many years member of the city board of health; died Jan. 25, aged 85.

Gans, Otto ✠ Port Chester, N. Y.; Johann Wolfgang Goethe-Universität Medizinische Fakultät, Frankfurt-am-Main, Prussia, 1923; on the staff of the United Hospital, where he died Feb. 9, aged 56, of hypertensive nephrosclerosis.

Gardner, Jerome Tewksbury, Hemet, Calif.; Cooper Medical College, San Francisco, 1890; served during World War I; formerly ship's surgeon on passenger ships of the Grace Lines; died Feb. 4, aged 88, of cerebral vascular accident.

Ghent, Charles Harry ✠ St. Paul; Northwestern University Medical School, Chicago, 1911; member of the staff of St. John's Hospital, where he died Jan. 30, aged 66, of acute monocytic leukemia.

Gorton, Arthur V., Norwalk, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1928; for many years on the staff of the Metropolitan State Hospital; died Feb. 7, aged 60, of coronary arteriosclerosis.

Grabill, John Stanley ✠ Mount Airy, Md.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1921; died Jan. 30, aged 57.

Grisanti, Joseph Michael, Buffalo; University of Buffalo School of Medicine, 1937; member of the Medical Society of the State of New York; died Dec. 27, 1954, aged 46.

Gwynn, William Clarence ✠ Washington, D. C.; Georgetown University School of Medicine, Washington, 1898; formerly on the faculty of his alma mater; a director of the Riggs National Bank; for many years on the staff of the Georgetown University Hospital, where he died Feb. 6, aged 80, of arteriosclerotic heart disease.

Hamilton, William Francis ✠ Havre, Mont.; University of Vermont College of Medicine, Burlington, 1903; an associate member of the American Medical Association; past president of the Kiwanis Club; on the staffs of the Sacred Heart and Deaconess hospitals; died Feb. 1, aged 74, of heart failure.

Hayward, William Frank, East Brookfield, Mass.; Medical School of Maine, Portland, 1899; school physician; served as member of the board of water commissioners and board of library trustees; died Jan. 12, aged 81, of valvular heart disease.

Henney, Patrick Joseph ✠ McKees Rocks, Pa.; University of Louisville (Ky.) Medical Department, 1911; Temple University School of Medicine, Philadelphia, 1918; an associate member of the American Medical Association; at one time county coroner and state senator; died Feb. 1, aged 69.

Heyn, Daniel Samuel, Cincinnati; Medical College of Ohio, Cincinnati, 1895; county jail physician; served during World War I; later assistant surgeon in the U. S. Public Health Service; died Feb. 11, aged 80, of acute pulmonary edema and coronary heart disease.

Hoey, John Joseph, Providence, R. I.; George Washington University School of Medicine, Washington, D. C., 1909; an associate on the staffs of St. Joseph's and Roger Williams General hospitals; died in the Rhode Island Hospital Feb. 4, aged 76, of diabetes mellitus.

Irvin, Cyrus Hughes ✠ Champaign, Ill.; St. Louis College of Physicians and Surgeons, 1906; associated with Burnham City Hospital and the Mercy Hospital, where he died Feb. 21, aged 76, of coronary occlusion and arteriosclerosis.

Jacobs, Merrill Ralph ✠ Chicago; Rush Medical College, Chicago, 1925; died in the Veterans Administration Hospital, Hines, Ill., Feb. 27, aged 54.

John, Ralph Chauncey, Albany, N. Y.; University of Kansas School of Medicine, Kansas City, Kan., 1931; served during World War II; associated with many Veteran Administration hospitals; died in the Veterans Administration Hospital Nov. 14, 1954, aged 60, of cerebral thrombosis.

Karn, Bert Ruthvin, Ortonville, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1907; city health officer; associated with the Ortonville Municipal Hospital; died in Minneapolis Jan. 4, aged 72, of coronary arteriosclerosis.

Kinney, Burton Oreno, Plainfield, Conn.; McGill University Faculty of Medicine, Montreal, Canada, 1916; died Nov. 25, 1954, aged 67.

Kirk, George P. ✠ East Grand Forks, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1896; city health officer; on the staffs of the Deaconess and St. Michael's hospitals; died Jan. 20, aged 80, of osteitis deformans.

Schlier, Earle Brooks, Bethlehem, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1919; member of the Medical Society of the State of Pennsylvania; on the staff of the St. Luke's Hospital; died Feb. 7, aged 59, of coronary occlusion.

Shapira, Abraham ✠ Pittsburgh; Maryland Medical College, Baltimore, 1912; Bennett Medical College, Chicago, 1914; died Jan. 26, aged 65, of coronary disease.

Shell, Roy Ellis, Van Wert, Ohio; Ohio State University College of Medicine, Columbus, 1930; died in St. Petersburg, Fla., Jan. 31, aged 51, of coronary disease.

Smith-Baker, Alice Walter, Long Beach, N. J.; Woman's Medical College of Pennsylvania, Philadelphia, 1905; medical missionary to China for many years; died in the Temple University Hospital, Philadelphia, Jan. 25, aged 77.

Turner, Wiley E. ✠ Piggott, Ark.; Memphis (Tenn.) Hospital Medical College, 1908; part owner of the Piggott Hospital; died Feb. 3, aged 78, of a heart attack.

Tyzzer, Robert Neal ✠ La Jolla, Calif.; National University of Arts and Sciences Medical Department, St. Louis, 1912; member of the Missouri State Medical Association; for many years practiced in St. Louis, where he was on the staff of the Missouri Baptist Hospital; died in the Scripps Memorial Hospital Jan. 20, aged 66, of chronic glomerulonephritis and uremia.

Vaughan, George Washington ✠ Wilmington, Del.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1917; past president of the New Castle County Medical Society; on the staff of the Wilmington General Hospital; died Feb. 11, aged 62, of myocardial insufficiency and coronary arteriosclerosis.

Ward, William Rankin ✠ Newark, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1893; for many years medical director of the Mutual Benefit Life Insurance Company; died in the Presbyterian Hospital Feb. 10, aged 84, of cerebral thrombosis.

Weiss, Samuel, Mill Valley, Calif.; Cornell University Medical College, New York, 1909; died in St. Francis Hospital in San Francisco Jan. 9, aged 70, of carcinoma of the pancreas.

Welch, Francis Joseph ✠ Portland, Maine; Medical School of Maine, Portland, 1906; specialist certified by the American Board of Internal Medicine; member of the American College of Chest Physicians and the American Trudeau Society; fellow of the American College of Physicians; associated with the Maine General and Mercy hospitals; died Feb. 10, aged 75, of coronary arteriosclerosis.

White, John Ira, Cleveland; Meharry Medical College, Nashville, Tenn., 1905; formerly medical director of the Ohio State Penitentiary in Columbus; died in the Lakeside Hospital Jan. 12, aged 70.

White, Landon Wilmer, Suffolk, Va.; Medical College of Virginia, Richmond, 1906; served during World War I; helped to establish the Virginia Hospital; for four years was health officer; a director of the Farmers Bank of Nansemond; died in the Louise Obici Memorial Hospital Feb. 6, aged 75, of thrombosis.

Whited, Elbert Patton ✠ Honaker, Va.; Medical College of Virginia, Richmond, 1903; died in Mattie Williams Hospital in Richlands Jan. 23, aged 82, of coronary thrombosis.

Williams, William Warren ✠ Quincy, Ill.; State University of Iowa College of Medicine, Iowa City, 1884; fellow of the American College of Surgeons; past president of the Adams County Medical Society; in 1934 was honored by the society at a banquet observing his 50th anniversary of medical practice; for many years associated with the Blessing Hospital, where he was on the honorary medical staff, and where he died Feb. 12, aged 93, of generalized arteriosclerosis.

Woodbury, Frank Thomas ✠ Colonel, U. S. Army, retired, New Rochelle, N. Y.; Medico-Chirurgical College of Philadelphia, 1899; entered the regular Army in April, 1901; promoted to lieutenant colonel in August, 1917; retired Sept. 9, 1922; became a colonel June 21, 1930; served in the Boxer Rebellion and the Philippine Insurrection campaigns, and during World War I; died Dec. 20, 1954, aged 79.

Workman, William McCullough ✠ Mount Joy, Pa.; Jefferson Medical College of Philadelphia, 1912; past president of the Lancaster City and County Medical Society; served during World War I; for many years deputy coroner in the Mount Joy area and company surgeon for the Pennsylvania Railroad; served as a director of the joint board of the Tuberculosis Society of Lancaster County and Rossmere Sanatorium in Lancaster; died in the Lancaster (Pa.) General Hospital Feb. 5, aged 71, of cor pulmonale.

FOREIGN LETTERS

BELGIUM

Committee on Documentation of Military Medicine.—At the 14th International Congress of Military Medicine and Pharmacy at Luxemburg and at Vianden in November, 1954, the International Committee on Documentation held its 17th meeting. Gen. Radmilo Jovanovic of Yugoslavia said that in the future it will be impossible for a state to insure the protection of an enemy's military medical personnel. An International High Commission in charge of the control and application of the principles of the Geneva Conventions should be formed, thereby subordinating national interests to the interests of humanity in general. Because it is becoming increasingly difficult to distinguish between the military and civilian medical service in wartime, universal laws governing these bodies should be formulated. A greater effort should be made toward the establishment of an International Medical Code. Medical assistance from neutral countries is indispensable in civilian and military prison camps, in territory occupied by the enemy, and in food inspection.

ENGLAND

Poliomyelitis Research.—Two years ago the National Fund for Poliomyelitis Research, a purely charitable organization, was established. During its second year it has quintupled its allocations for research projects. The greater part of this sum—just over $89,600—has been devoted to research into the cause and prevention of poliomyelitis, only about 10% being allocated to research into treatment of the disease. This differentiation is deliberate, as it is believed to be much more important to concentrate on prevention rather than cure. Of the sum allocated to treatment, $2,800 has been allocated for the building of four special rocking beds for research on the improved treatment of respiratory failure due to poliomyelitis. A grant has also been made for the construction of four Darcus strain-gauge dynamometers. This is an apparatus devised by Dr. H. D. Darcus of the Medical Research Council's research unit on climate and working efficiency at Oxford. It is intended for the quantitative assessment of muscle power and will be used in an investigation into the relative value of moderate and intensive activity in the treatment of peripheral paralysis. A feature of the fund's policy is that full consultations are held with the Medical Research Council before any grants are made for research work. Partly as a result of this stimulation, the Medical Research Council has now reorganized the planning of its activities in the field of poliomyelitis. It has appointed three expert working parties to deal, respectively, with: (1) the laboratory aspect, which includes research into developing a safe and effective vaccine; (2) the treatment of the bulbar form of the disease, by means of improved models of iron lungs and other apparatus to assist the patient's breathing; and (3) the treatment of the paralyzed limb.

Nurses Should Close Surgical Wounds.—According to Sir Heneage Ogilvie, consultant surgeon to Guy's Hospital, "A great deal of every operation consists in stitching, an art in which a surgeon has not been trained, that he attempts for the first time as an adult, and that he never learns to do really well. Yet by his side, veiled and voiceless, is a girl who has been stitching since she could toddle and who could do the job more neatly than he can, and in half the time. Operations would be done much better if the surgeon, having explored, decided, mobilized, and resected, were to hand over reconstruction and closure to a nurse working under his direction, leaving to her the fashioning of the anastomosis, the recovering of raw area, and the closure of the wound."

Distribution of Medical Personnel.—The British Medical Association recently analyzed the type of work done by 58,600 physicians in Great Britain; 23,200 are engaged in general practice, 19,000 work in hospitals or in university medical schools (this figure includes 6,650 specialists and 1,500 physicians on university staffs), 3,400 are public health medical officers of whom 600 are in the government service and 400 are in industry, 250 are employed by the Medical Research Council, and 6,900 are partially or wholly retired. Of the total, 47,700 are men and 10,900 are women; of these, 4,200 men and 400 women are over 70 years of age.

FINLAND

Breast Feeding.—On the initiative of pediatricians attached to the University Children's Hospital in Helsinki the health authorities in Helsinki issued questionnaires on breast feeding to be filled in by the public health nurses in the child welfare centers. The information thus obtained is reported in *Nordisk medicin* for Nov. 11, 1954. Of over 6,000 infants born in Helsinki in 1952 information was obtained on 2,597, and of these only 37% had been breast fed for more than three months, and only 15% for more than six months. These findings showed a marked deterioration in the situation as compared with previous investigations. The fear of summer diarrhea may partly account for the fact that breast feeding lasted a little longer for infants born in the spring and summer than for those born in the other seasons. The older the mother, the longer was the duration of breast feeding. Many factors were found to influence the duration of breast feeding. Its discontinuation was due to mastitis in 8.6%, some other illness of the mother in 9.6%, debility or illness of the infant in 2.2%, and employment of the mother outside her home in 9.9%. No definite cause for the discontinuation of breast feeding could be found in many cases. The most important factor appeared to be the mother's attitude toward breast feeding, and this is a phenomenon difficult to analyze.

TURKEY

Progressive Dementia Paralytica.—In *Saglik Dergisi* (vol. 24, no. 7) Dr. Faruk Bayülkem of the Istanbul-Bakirköy Mental Hospital discussed the results of a 16-year investigation of the blood and spinal fluid of 6,137 patients in relation to the syphilitic origin of mental diseases and analyzed the symptoms of the 382 patients with progressive dementia paralytica. In order to arrive at a diagnosis when patients are not hospitalized, the presence of syphilis is frequently determined solely on the basis of the serologic test. In 14.5% of 6,137 such tests, however, the Wassermann and Kahn reactions were negative or only faintly positive in patients whose mental disease was of syphilitic origin and who had strongly positive Wassermann and Kahn reactions of the spinal fluid. In the 328 patients with progressive dementia paralytica, periosteum, bone, and tendon reflexes were normal in 18% and dysarthria and tremor of the tongue were absent in 16%. The spinal fluid cell count of three patients observed for three years was 125 to 150 per high-power field before the induction of malaria. After three malarial chills followed by specific chemotherapy, the spinal fluid cell count still averaged 30 cells per high-power field and the spinal fluid Wassermann remained strongly positive, an important prognostic point. The author recommended further malarial chills, and he stressed the importance of the histopathological interrelation of the spinal fluid and the brain.

The items in these letters are contributed by regular correspondents in the various foreign countries.

GOVERNMENT SERVICES

ARMY

Dr. Churchill Delivers the Keller Lecture.—Dr. Edward D. Churchill, chief of the general surgical services, Massachusetts General Hospital, Boston, delivered the third annual William L. Keller Lecture, March 17, at the monthly meeting of the Army Surgeon General in the Walter Reed Army Medical Center. Dr. Churchill discussed gunshot wounds. The William L. Keller Lecture has been established by the Surgeon General, as an annual lecture in honor of Col. William L. Keller, who made outstanding contributions in the field of surgery while on duty at Walter Reed Army Hospital following World War I.

NAVY

Training Films Receive International Recognition.—Two awards for Navy training films entered in the International Exhibition of Cinematographic Art held annually in Venice, Italy, were recently received in the Navy Department. The award-winning films, entitled "Breathe and Live" and "Equilibration of Occlusion," were produced by the Bureau of Aeronautics under the direction of the Audio-Visual Training Section, Bureau of Medicine and Surgery. The awards are on display at the Naval Photographic Center, Anacostia, D. C., with other previous awards for excellence of training films that have been received by the Navy's Bureau of Medicine and Surgery. The Bureau of Medicine training film awards were received in an international exhibition where only the best entries of training film productions are accepted.

Personal.—The National Board of Medical Examiners on Feb. 25 invited Rear Adm. Batholomew W. Hogan, the Navy's Surgeon General, to serve as a member of the board.——Rear Adm. Irwin L. V. Norman has assumed the duties of Assistant Chief for Personnel and Professional Operations, Bureau of Medicine and Surgery, relieving Rear Adm. John Q. Owsley who will report for duty as commanding officer of the U. S. Naval Hospital, Oakland, Calif. Capt. Donald James O'Brien, Naval Reserve, relieved Capt. Marvin H. Porterfield, M. C., U. S. N. R., as director of the Naval Reserve Division, Bureau of Medicine and Surgery, on March 1. Captain Porterfield, who was released to inactive duty, will reside in Martinsburg, W. Va., where he will engage in the private practice of medicine to a limited extent and operate his farm.

VETERANS ADMINISTRATION

New Hospital Managers.—Dr. Michael L. Matte, manager of the Denver VA Hospital, has been transferred to manage the 516-bed VA Research Hospital in Chicago, succeeding Dr. William W. Fellows, who was promoted and transferred to Washington, D. C., as Assistant Chief Medical Director for Planning in VA's Department of Medicine and Surgery. Replacing Dr. Matte as manager of the 504-bed Denver VA Hospital is Dr. Harold M. Engle, manager of the 194-bed general medical and surgical hospital in Salt Lake City. Dr. Thomas O. Lake, chief of professional services at the VA Hospital in Oakland, Calif., has been promoted to manager of the Salt Lake City hospital, replacing Dr. Engle.——Dr. Daniel R. Robinson, chief, professional services, VA Hospital on West 10th St. in Indianapolis, has been appointed manager of the VA hospital in Dwight, Ill., succeeding Dr. Joseph L. Campbell, who resigned last November. Dr. Robinson entered military service in 1942, serving in the Air Force. He was separated in 1946 and returned to Baltimore to practice medicine. He joined VA in April, 1953, as assistant chief of professional services in the VA hospital at Fort Howard, Md.

PUBLIC HEALTH SERVICE

Training for Emergencies.—A series of training courses for physicians and other professional health personnel who would be called to duty in the event of enemy action or other national emergency has been announced by the Public Health Service. For two weeks, beginning March 14, about 50 medical officers, sanitary engineers, nurses, and dentists from 24 states convened in Washington for training in chemical, biological, and radiological warfare defense and emergency health and sanitation activities. Each trainee is a member of the Commissioned Reserve Corps of the Public Health Service and is attending the training course as part of the service's emergency program to expand its Commissioned Reserve by 5,000 new officers by July 1, 1956.

During the first week, the trainees spent three days at the Federal Civil Defense Administration Staff College at Olney, Md., for briefing on the strategic aspects of civil defense. The remainder of the period was spent at Public Health Service headquarters in Washington. A second two-week course has been scheduled for May 15 for another group of Commissioned Reserve officers. Additional courses will be scheduled later. The courses fall into two main categories: The first category deals with problems with which a health department staff is generally familiar but for which additional help is required, such as extensive disruption of public facilities and health problems involved in mass displacement of civilians resulting from enemy action or natural disaster. The second category is concerned mainly with unusual problems for which new skills as well as additional help are needed by a health department, such as chemical, biological, and radiological warfare defense, epidemic reporting, monitoring radiological fall-out, decontamination, and related problems.

MISCELLANEOUS

Study of Civil Defense for the Food Industries.—A Civil Defense Foods Advisory Committee has been established by the National Academy of Sciences, National Research Council, at the request of the Food and Drug Administration. The committee will study the vulnerability of the food processing and warehousing industries to attack or sabotage by biological, chemical, or radiological agents. The committee will be concerned also with methods and facilities for sanitizing or decontaminating food plants, equipment, and products in a civil defense emergency. The committee is composed principally of food industries men, but the members are not serving as representatives of their companies or institutions. Roy C. Newton, vice-president, research, Swift and Company, Chicago, is chairman. As is customary under Academy-Research Council policy, the members are serving without compensation. The committee's first meeting, in Washington, Feb. 18-19, was devoted largely to briefings of members by representatives of governmental agencies. The initial task will be to review all pertinent information. In this effort the committee anticipates helpful assistance from others in the food and allied industries and in civil and military defense agencies.

The National Academy of Sciences is a private nonprofit corporation electing its own members from the leading scientists in the United States. It was established by Act of Congress, approved by President Lincoln, March 3, 1863, for the furtherance of science and to advise the government on request in scientific and technical matters. The National Research Council was organized by the academy in 1916, with the cooperation of the major scientific and technical societies, to enable scientists and engineers to associate their efforts with those of the limited membership of the academy in service to science and to the government. The Food and Drug Administration in the Department of Health, Education, and Welfare enforces federal laws to insure the purity, safety, and truthful labeling of foods, drugs, and cosmetics.

MEDICINE AND THE LAW

This is the last in a series of four articles dealing with the federal income tax law as it affects physicians. Reprints of the series published in booklet form under the title "Federal Income Tax Liability of Physicians" may be had without charge from the Law Department, American Medical Association, 535 N. Dearborn St., Chicago 10, Ill.—ED.

FEDERAL INCOME TAX: TAX ASPECTS OF A MEDICAL PARTNERSHIP

Partners are liable for federal income tax as individuals, and each should report his share of partnership income or loss together with other items of income or loss in determining his taxable income. The partnership itself is an entity not subject to income tax although it is required to file an information return and report its income The partnership as an entity, rather than each individual partner, has the option in its first taxable year to account for income on a cash basis (as fees are received and expenses actually paid) or on an accrual basis (as fees are earned and expenses incurred, although not necessarily paid). Medical partnerships, like individual practitioners, customarily use the cash basis since there is no advantage in paying income tax on professional fees until actually received. Further, in using the cash basis a taxpayer may control his taxable income, to a limited extent, by paying bills in the current year or by postponing the payment of such bills until the following year. The partnership, as an entity, computes the depreciation deduction on depreciable partnership property in arriving at partnership income. The individual partners do not separately compute depreciation on their respective shares of partnership property.

As under the former law, partners are liable individually for income taxes on their shares of partnership income, in accordance with the partnership agreement, which may provide for different distributive shares of any item of gain, loss, deduction, or credit. However, the new law provides that any such provision in an agreement will be disregarded if the principal purpose is income tax avoidance or evasion. The distribution ratio for taxable income or loss, exclusive of the items required to be treated separately, would then be applied. Frequently, medical partnership agreements provide only for the division of professional fees, after payment of expenses, without reference to the other items. Where no provision is made for the division of particular items, each partner's distributive share of such items will be determined in accordance with his distributive share of ordinary income or loss.

Illustration.—The partnership agreement of Drs. A and B provides that they will share in partnership income, 60% for Dr. A, the senior partner, and 40% for Dr. B, the associate partner. Each originally contributed $10,000 to the partnership. Taxable income for the year amounted to $60,000, which included $50,000 from professional fees after deducting expenses and $10,000 in long term capital gain. Dr. A's 60% share of regular partnership income is $30,000, and Dr. B's is $20,000. Inasmuch as no special provision was made in the partnership agreement for the treatment of capital gains the same percentage ratio used in dividing partnership net income will be used in allocating the capital gain. Dr. A will report $6,000 in capital gain and Dr. B, $4,000. In view of the equal investment in the partnership, it is possible that an equal division for capital gains might have been agreed on if it had been considered in preparing the partnership agreement.

When the partnership agreement provides for a different ratio for sharing regular professional income than that applicable to the sharing of losses—and there is no provision as to the division of other items of income—the professional income ratio is applicable if the partnership has taxable income in the particular taxable year, and the loss ratio is applicable in any year in which the partnership has a loss.

The 1954 Code provides numerous technical and procedural and some substantive changes in the income tax law as it relates to partnerships. Many of these, although important to businessmen, are of little concern to doctors. Only the principal provisions affecting medical partnerships are covered here. Generally, the new partnership provisions of the 1954 Code apply to partnership taxable years beginning after Dec. 31, 1954. Some of the new provisions have a special effective date. These will be indicated when applicable. The 1939 Code still applies to partnership taxable years beginning before Jan. 1, 1955, and any part of a partner's taxable year falling within such partnership taxable years. When the 1939 Code requires a different taxing procedure, this will be shown.

Formerly partners could defer tax liability in connection with income from a new partnership for as long as 11 months by adopting a tax year for the partnership different from the partners. After April 1, 1954, a new partnership may not adopt, nor may an existing partnership change to a tax year other than that of its principal partners. A principal partner, for this purpose, is one having an interest of 5% or more in the partnership profits or capital. However, by application to the Commissioner, a partnership may adopt or change to a tax year other than that of all its principal partners if a satisfactory business purpose for the desired change can be established.

CONTRIBUTIONS TO PARTNERSHIP

Nonrecognition of Gain or Loss.—No gain or loss is recognized either to the partnership or to any of its partners on a contribution of property to a partnership in exchange for a partnership interest. This rule applies both in the case of a contribution to a partnership in the process of formation and in the case of a contribution to a partnership that is already formed and operating.

Basis.—The "basis" of property contributed by a partner to a partnership is its cost to him. The "adjusted basis" of property is determined by making adjustments to its cost. Improvements and betterments to the property and other costs chargeable to the capital account during the time it was held are added. Items that amount to a recovery of a part of the cost, such as depreciation, are deducted. The basis of a partner's interest, in a partnership acquired in exchange for a contribution of property and/or money, is the amount of money contributed plus the "adjusted basis," to the contributing partner, of any property contributed. The basis to the partnership of property contributed by a partner is the "adjusted basis" of such property, to the contributing partner, at the time of the contribution. In other words, property contributed to a partnership has the same basis to the partnership for purposes of determining gain, loss, depreciation, and so forth as it has to the contributor.

Illustration.—Drs. A and B organize a partnership to which each contributes property having a fair market value of $10,000. Dr. A contributed property that cost him $8,000. Dr. B contributed property costing him $13,000. The basis of the property is not the market value, but the same basis it had to the partners, $21,000. The basis to Dr. A of his partnership interest is $8,000, and the basis of Dr. B's partnership interest is $13,000.

Partners' Contributions.—Generally, the 1954 Code corresponds to the old law in respect to partners' contributions to a partnership. Unless another provision is made in the partnership agreement, items of income, gain, loss, deduction, or credit, with respect to property contributed by a partner, are allocated among the partners in the same manner as similar items arising with respect to property purchased by the partnership. In other words, an allocation will be made according to the partners' normal ratio of dividing profits and losses. For example, if a partner contributes property to a partnership with an adjusted basis less than its value at the time of contribution, the gain on the sale of such property by the partnership will be taxable to each of the partners in accordance with his distributive share

of gains just as if the property had been purchased by the partnership. The fact that one partner may gain a tax benefit while his partners sustain a tax disadvantage is immaterial. However, if provision is made in the partnership agreement for sharing depreciation or gain or loss on contributed property among the partners so as to take account for the variation between the basis of the property to the partnership and its market value at the time of contribution, the partnership agreement will apply. While the rule may result in possible detriment (or gain) to the partners who did not contribute the specific property sold, there will generally be a corresponding loss (or gain) to such partners on the sale or disposition of their interest in the partnership.

Illustration.—Drs. A and B are equal partners in a partnership to which Dr. A contributed a small office building having a market value of $20,000 and Dr. B contributed $20,000 in cash intended to be used for remodeling and installing new equipment. Their partnership agreement is in simple form and provides only for a division of profits. After commencing their partnership practice, the doctors realize that the premises are inadequate, sell the building for $20,000, and rent other office facilities. Dr. A had purchased the property several years before for $10,000. Its agreed market value was $20,000 at the time the partnership was formed. Under the 1954 Code, the basis to the partnership for figuring gain or loss on property contributed by a partner is the cost of the property to the contributing partner, after allowing for certain items of adjustment, such as deductions for depreciation and additions for capital improvements. Neither Dr. A nor Dr. B had even considered Dr. A's basis in their partnership negotiations. The 1954 Code provides that gain or loss with respect to property contributed by a partner shall be allocated between partners in accordance with their partnership agreement. The agreement between Drs. A and B calls for an equal division of profits. When their accountant prepares the partnership return after the end of the partnership year, Dr. B finds that the partnership realized a gain of $10,000 on the sale of the property, his share being a capital gain of $5,000. Dr. B thus found himself faced with an unforeseen tax liability. If the partnership was liquidated (assuming no other transactions) each of the partners would receive $20,000. For tax purposes, the cost basis of Dr. B's partnership interest would be $20,000 plus $5,000 (the amount of his share of the so-called gain on the sale of the property contributed by Dr. A) or $25,000. He would therefore have a $5,000 loss in the event of liquidation, if there were not other items of income or loss to be considered.

It can be seen from the above illustration that failure to anticipate tax consequences in the formation of what might be assumed to be a routine partnership, resulted in a tax inequity. The injured partner is entitled to a tax credit that he can use only in the event of liquidation of the partnership, but partnerships are not formed in contemplation of imminent liquidation. Situations of this type may be avoided by inserting an appropriate provision in drafting the original agreement or by amending an existing partnership agreement. Under a provision of that type the gain could be shared between the partners so as to take account of the variation between the basis of the property to the contributing partner and the valuation at which it is contributed to the partnership. If a provision of this type had been contained in the agreement in the illustration, Dr. A would have been chargeable for the entire tax on the $10,000 gain and Dr. B would have been chargeable with none of this gain.

DEALINGS BETWEEN PARTNER AND PARTNERSHIP

The 1954 Code provides that for partnership years beginning in 1955 and thereafter, a partner dealing with the partnership, other than in his capacity as a partner, will be treated as if he were an outsider. Common transactions include the sale of property by the partner to the partnership, the purchase of property by the partner from the partnership, and the rendering of services by the partner to the partnership or by the partnership to the partner. These transactions are distinguished from those in which a partner contributes money or property to the partnership in exchange for a partnership interest or receives distributions of money or property from the partnership. This approach is consistent with the concept of the partnership as a separate "entity." Therefore, a partner who sold property to a partnership of which he is a member may be taxed on the entire gain or may deduct the entire loss, within certain limitations. An exception to this general rule is made in sales of property between the partnership and a controlling partner. Deductions for losses on the sale of property between a partnership and a partner owning more than 50% of the capital or profits interest in such partnership are disallowed. Also, gain on the sale of property shall be recognized as ordinary gain (not capital gain) if the sale takes place between a partnership and a partner owning more than 80% of the capital or profits interest in such partnership. In both instances, the partnership interest of close relatives, such as a father, son, or brother, are included with the interest of the partner making the sale in determining whether the latter's partnership interest exceeds the percentage limitation.

Illustration.—Drs. A, B, and C, who are not related, are equal partners. Dr. A sells an office building to the partnership for $30,000. His basis was $21,000. The total $9,000 gain is taxable. Since the partnership is considered a separate entity, any claim that he is dealing with himself to the extent of his interest in the partnership, and that therefore only $6,000 gain was realized, would not be recognized under the 1954 Code.

Payment of Salaries to Partners.—Sometimes a senior physician who takes in a junior or associate physician as a partner will provide him with a guaranteed "salary" in addition to a small partnership interest. Such salaries are not subject to social security taxes or the withholding provisions that are applicable to bona-fide employees. In connection with partnership years beginning before 1955, the guaranteed salary is treated the same as any other distribution of partnership profits. However, for partnership years beginning in 1955, a partner receiving a guaranteed salary from a partnership is treated as an outsider or stranger, and the partnership is allowed a business deduction for such salaries paid. The payment of such a salary, if it is to be allowable as a business deduction by the partnership, must be mandatory and not contingent on the existence of partnership profits. If the partner's salary is not in fact guaranteed, it will be treated as a regular distribution of profits, as under the prior law. It should be noted that guaranteed salary payments should be reported by the recipient, for tax purposes, at the end of the partnership year in which they are paid, and, at the same time, he reports his share of the partnership profits.

SALE OF A PARTNERSHIP INTEREST

Under both the 1954 Code and the 1939 Code, a physician who sells his partnership interest at a profit is taxed, generally, at capital gain rates rather than the higher rates applicable to ordinary income. The sale is treated in the same general manner as the sale by a stockholder of shares of stock in a corporation. This favorable tax treatment is based on the premises that an interest in a partnership is a capital asset although there is a conflict. Some of the court cases decided under the old law included as capital gain that portion of the sales proceeds attributable to the partnership's "unrealized receivables" or uncollected income.

Unrealized Receivables.—After March 9, 1954, a partner who sells his interest in a partnership has ordinary income and not a capital gain to the extent that the sales proceeds for his interest are attributable to the partnership's unrealized receivables.

Illustration.—Drs. A and B each have a cash investment of $5,000 in an equal partnership. Unrealized receivables (uncollected fees not reported as income) amount to $6,000. By mutual agreement, in January, 1955, Dr. A sells his entire partnership interest, including his share of uncollected fees (½ of $6,000, or $3,000) to Dr. C for $15,000. The basis of Dr. A's partnership interest is $5,000. His gain is allocated as follows:

Selling price of Dr. A's partnership interest	$15,000
Less cost basis	5,000
Total gain	$10,000
Less allocable share paid for unrealized receivables (ordinary income)	3,000
Balance, or capital gain	$ 7,000

PAYMENTS TO RETIRING OR DECEASED PARTNER

When a partner retires or dies and payments are made by the partnership to the partner or his heirs, the amounts so paid may represent several items. They may, in part, represent the withdrawing partner's capital interest in the partnership. They may include his pro rata interest in unrealized receivables or uncollected fees of the partnership. The 1939 Code contained no provisions relating to the tax treatment of such payments, and the case law developed by court decisions offered no consistent approach. Under the 1954 Code, payments in excess of the value of the partner's capital interest in the partnership are ordinary income (not capital gain) to a retiring partner or a deceased partner's heirs and are deductible from the partnership income of the remaining partners. However, in computing the value of a partner's capital interest, his share of the following are not included: (1) unrealized receivables or uncollected fees not reported as income and (2) good will of the partnership, except to the extent that the partnership agreement provides for a payment with respect to good will.

Payments for capital interest provide the remaining partners with no deductions, but they make it possible for the recipient to receive the preferential tax treatment afforded to capital gains. On the other hand, payments representing participation in partnership income may be deducted by the remaining partners, but the recipient is taxable on such payments as ordinary income.

Illustration.—Drs. A, B, and C are partners. The basis of Dr. A's partnership interest is $5,000, which is also the fair market value of his share of the partnership's physical assets. No provision is contained in the partnership agreement with respect to a payment for good will in the event of the retirement or decease of a partner. Dr. A retires and is paid $25,000 for his partnership interest by the partnership. Of this amount, $5,000 will be considered payment for Dr. A's capital interest and $20,000 ordinary income. The remaining partners will have a deduction of $20,000.

If a provision had been made in the partnership agreement for a payment with respect to good will, Dr. A could have had the benefit of a capital gain. Such a change could have been made in the partnership agreement at any time up to the consummation of the arrangements for Dr. A's retirement. However, a payment with respect to good will would not have been deductible to the partnership. Accordingly, the acquisition of the tax benefits of capital gain to the retiring partner can be weighed against the relinquishment of the deduction to the remaining partners, with an appropriate adjustment made therefor in the amount paid to the retiring partner.

CONCLUSION

One of the economic reasons that sometimes motivates a physician to enter into a medical partnership is the objective of creating a valuable professional interest that will have monetary worth to his heirs and to the remaining partners in the event of his retirement or death and for which they are willing to make payment. Consequently great care should be exercised in the preparation of a new partnership agreement, and it should be reviewed from time to time and amended, if necessary, in order to keep abreast of changing circumstances among the partners and developments in the tax law. The 1954 Code refers to the "partnership agreement" in no less than six instances in connection with the tax status of partnership transactions. The new partnership provisions provide partners with a wide degree of latitude in making an equitable division of the total partnership tax liability among themselves. Partnership agreements may be changed at any time up to the original due date of the partnership return, and the changes made will affect the tax liability of the partners for the taxable year. Although designed to give partners flexibility in determining each partner's fair share of the entire tax responsibility, these same provisions may lead to tax inequities among the partners if ignored.

This article is not intended as an aid to physicians in solving their own tax problems arising out of the partnership participation. It is intended only to alert the physician to the fact that there are special tax consequences incident to partnership and assist him in discussing the subject intelligently with his tax advisor or attorney.

MISCELLANY

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PHYSICIAN'S PRAYER

Lord, Who on earth didst minister
To those who helpless lay

In pain and weakness, hear me now,
As unto Thee I pray.

Give to mine eyes the power to see
The hidden source of ill,

Give to my hand the healing touch
The throb of pain to still.

Grant that mine ears be swift to hear
The cry of those in pain;

Give to my tongue the words that bring
Comfort and strength again.

Fill Thou my heart with tenderness,
My brain with wisdom true

And when in weariness I sink
Strengthen Thou me anew.

So in Thy footsteps may I tread,
Strong in Thy strength alway;

So may I do Thy blessed work
And praise Thee day by day.

Reproduced with permission from the Illinois Medical Journal *(June, 1953).*—Ed.

"AMERICA"

Oh, land of vast and fertile fields
Two oceans lap your shores
A hungry world depends upon
The crops your harvest yields.

Your mountains so majestic,
Their summits capped with snow
Are challenged by your cities
With giants all aglow.

Your rivers flow down to the sea
And on their bosom carry
Great wealth of man-made luxury
A world essential ferry.

Your peoples came from everywhere
To fuse a mighty nation,
And hand in hand a freedom share
The noblest in creation.

And yet "Colossus" in your might
Twice have you thrown your weight
Into the scale of Peace and Right
And saved the world from Fate.

May God in all His Greatness
Wherever He holds court
Keep His arms around your shoulders
And yield you His support.

America, America, stay virile
Young and strong
Let history immortalize, your
Courage and your song.

Robert Sixtus Berghoff, M.D.

THE LEISURE CORNER

MEDICAL HISTORY AS A HOBBY

Some decades ago Sir William Osler told his colleagues: "No man is really happy or safe without a hobby, and it makes precious little difference what the outside interest may be—botany, beetles or butterflies, roses, tulips or irises; fishing, mountaineering or antiquities—anything will do so long as he straddles a hobby and rides it hard." And on another occasion he said: "In the continual remembrance of a glorious past individuals and nations find their noblest inspiration." Thus Osler expressed his own continuous preoccupation with the history of medicine and derived his inspiration from his favorite hobby.

It is not surprising that many thoughtful physicians have shared his predilection. In the course of their daily activities, be they research, practice, or the teaching of medical students, doctors are bound to be confronted with the ever-recurring questions: "Who did this first?"; "How did that develop?"; and "How did it all come about?" Obviously, the medicine taught and practiced in the 20th century is not a spontaneously generated science but is the result of a long evolution. The history of medicine is a key to the understanding of this evolution. The majority of physicians who have turned historians have done so in search of their own medical roots, and they have found that—almost inadvertently—this search has widened their horizons and increased their understanding of medicine as a whole. Just as the educated man alone can be a well-integrated person, so only a physician acquainted with the historical and humanistic relations of medicine to society can be a completely integrated practitioner of medicine.

Apart from its educational value, medical history is attractive as an extra-vocational interest of the doctor, because it does not require much special preparation, equipment, or extensive time. Medical books, belletristic literature, and even the poetry of the past abound in sources for any phase in the history of medicine, in which the physician might find himself interested. Finally, this of all hobbies lends itself to the years of declining physical activity; and in the years of retirement from active participation in medicine, a student of medical history can greatly enrich his remaining years. Conversely, the contemplative and reminiscent periods may mellow and enrich the historical evaluations.

The broad term "medical history" embraces a wide variety of subdivisions, one or more of which should appeal to virtually any physician. Not only the evolution of medicine as a whole is included but the study of specific periods in history, the development of the individual disciplines or specialties, the lives of great personalities in medicine, the treatment of a specific disease, or the development of a certain instrument are all phases worthy of historical investigation. In addition, the relation of medicine to art, to literature, to political history and even to religion provides directions into which one's interest may grow. The medical history of the doctor's own community or country can constitute a fruitful and enjoyable source of historical investigation.

Concern with local history as well as the history of American and British medicine obviates entirely the necessity of grappling with texts in foreign or classical languages. But even in regard to the medicine of foreign countries and ancient periods there is little need for getting involved in the study of the languages in which the original texts were prepared. A great many excellent translations, often accompanied by facsimile reproductions, are readily available for most of the significant milestones in medical history.

In spite of the vast and rich literature in the field, there still remain many unexplored areas and unsolved problems awaiting further study. It is fortunate, therefore, that many physicians feel impelled, after a preliminary period of reading, to carry out some research of their own and to prepare papers on some phase of medical history. The use of an historical introduction in the presentation of a clinical case at a hospital conference or even the preparing of a paper on some historical subject to be read at hospital staff meetings or local medical society meetings provide gratifying and stimulating responses. A step beyond, of course, is the participation in local or national societies devoted to the study of medical history and the preparation of papers to be presented before such bodies.

The question of the use of one's time is often brought up when interest in medical history is suggested. If the time so spent can be counted as recreational time then its use is not wasteful. It is an interesting observation that among those who have most contributed to the history of medicine over the years, very many have been just those physicians who have attained real distinction in their own specific fields of medicine. Conversely stated, among the men who have made their mark in medicine one finds a large representation of students of medical history. Among the many who can be mentioned in this respect are Virchow, Ehrlich, Osler, Welch, Halsted, James B. Herrick, and many, many others.

One vista that the student of medical history finds open to him is the fellowship with kindred spirits. He not only can share his love of medical history with his contemporaries but can find discussion and study groups with students or members of the house staff mutually enjoyable, instructive, and stimulating. Sir William Osler long enriched his own experience and the lives of his young associates by evenings of discussion of various phases of the history of medicine.

Although the preoccupation with the history of medicine rarely stems from practical or material motives, there are occasional and unexpected rewards, resulting from the rediscovery of therapies and remedies that have been lost with the passage of time. Many such have already occurred. From among these mention may be made of quinine, cocaine, ephedrine, and the most recent find Rauwolfia serpentina, the "snake root plant" that has added so much to our modern pharmacopeia. A systematic study of the history of medicine would have revealed a number of practices that have been long in use before they were "discovered" for the second time. The ancient and medieval method of treating goiter with decoctions of seaweed antedated by millenia our recognition of the effect of iodine on the thyroid gland. Extract of toad venom was given to patients centuries before the synthesis of bufagin. The so-called "backward" peoples used mildewed bread for the cure of festering wounds long before the civilized world discovered its penicillin; and chaulmoogra oil, until recently the only therapeutic agent in the treatment of persons with leprosy, has an unbroken history in India that antedates the Christian era.

It is clear, however, that the study of medical history has values that go far beyond the tangible assets for modern medical practice and beyond the enjoyment of the individual history-minded physician. Thus, the feeling for the past is not only desirable but necessary for those who wish to practice in foreign countries. While this is true even for the physician who goes to another country within the sphere of Western civilization, historical knowledge is absolutely mandatory for those who wish to bring Western medicine to non-Western peoples. Very little can be done by forcing the blessings of 20th century medicine on an unwilling population; but much can be achieved by a subtle blending of indigenous beliefs with modern practice.

Even this cursory analysis shows the variety of functions filled by the history of medicine. No matter whether it is pursued for its inherent pleasure or for an ultimate purpose, historical awareness will give the physician a new perspective of his profession and will bring into focus his own accomplishments and the achievements of his time. Solutions may differ, but the basic questions have remained the same; each age had its own dread diseases and miracle drugs, its own form of science, and its problem of specialization. The satisfaction in knowing about the continuity of medical thinking is heightened by the awareness that the fundamental aims of medicine have always remained the same. The modern physician, like his ancient predecessor still proceeds along the Hippocratic maxim that "Life is short and the art is long; the occasion fleeting; experience fallacious, and judgment difficult. The physician must not only be prepared to do what is right himself, but he must also make the patient, the attendant and the externals cooperate."

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Sicklemia and Infarction of Spleen During Aerial Flight: Electrophoresis of the Hemoglobin in 15 Cases. E. W. Smith and C. L. Conley. Bull. Johns Hopkins Hosp. 96:35-41 (Jan.) 1955 [Baltimore].

The degree of sickling of the erythrocytes of individuals with sicklemia is known to be related to the oxygen tension to which the blood is exposed. Observations suggest that individuals with sicklemia might be adversely affected by exposure to reduced oxygen tension such as occurs during high altitude flight. Smith and Conley cite a report by Cooley and associates, which reported six Negro soldiers who experienced nausea, vomiting, pain in the left upper abdomen, and fever during prolonged flights in unpressurized aircraft at altitudes between 10,000 and 15,000 ft. All of the patients had been in apparently good health prior to the flights, and there was no history of previous manifestations of sickle cell disease. On examination there was pronounced left upper quadrant tenderness, paralytic ileus, fever to as high as 104 F, and leukocytosis. Laparotomy was performed in each case, and an enlarged, grossly infarcted spleen was removed. Since the report of Cooley and his associates, more than 15 additional patients with splenic infarction occurring during flight have been observed in military hospitals. In this paper the authors describe electrophoretic studies on sterile blood samples of these 15 patients. Sickle (S) hemoglobin was present in the blood of each of the 15 individuals who had developed splenic infarcts during flight. In three cases C hemoglobin was also present, indicating that these were instances of sickle cell–hemoglobin C disease. The remaining 12 persons had normal (A) hemoglobin in addition to the S component. In 11 of these cases, the amount of normal hemoglobin exceeded the amount of sickle hemoglobin. This is the pattern expected in the sickle cell trait. One patient had slightly more sickle than normal hemoglobin, and about 20% target cells were seen on the blood smear. It is not known whether this case is an instance of sickle cell trait or whether it may represent an unusual sickle cell–thalassemia or some other variant of sickle cell disease. None of the 15 patients had been suspected of having sicklemia prior to the hospitalization for splenic infarction. Of the three patients with sickle cell–hemoglobin C disease, one had recurrent leg ulcers as a child; none had a sickle cell habitus. The occurrence of splenic infarcts during flight in this rather large group of individuals with sicklemia suggests that this phenomenon is not rare. Evidently flying is hazardous to persons with sickle cell–hemoglobin C disease, because of the risk of splenic infarction. Splenic infarcts may develop during flight even in individuals who have only sickle cell trait.

Pulmonary Histoplasmosis. J. W. Middleton. J. Louisiana State M. Soc. 107:1-6 (Jan.) 1955 [New Orleans].

Histoplasmosis is an endemic, sometimes epidemic, disease prevalent in the Mississippi basin region. It is caused by inhalation of Histoplasma capsulatum from an exogenous source in nature. Instances of person to person transmission have not been reported and even prolonged contact with animals known to be infected has not resulted in human infection. The primary phase of the infection, which is pulmonary and in 95% of the cases asymptomatic, may progress into a chronic pulmonary disease or a disseminated infection or it may largely heal without significant damage. The diagnosis in asymptomatic patients is usually made retrospectively on the basis of multiple pulmonary calcification and a positive histoplasmin and a negative tuberculin reaction. Problems in differential diagnosis arise when the pulmonary infection assumes an active, acute or chronic, symptomatic form. The onset of the acute symptomatic illness is sudden, with malaise, fatigue, and muscular aching, followed in from 24 to 36 hours by a chill or chilliness, remittent fever, sweating, and constricting chest pain. Physical findings are variable and nonspecific. X-ray examination may be normal at first but soon shows extensive bilateral involvement of the lungs, with lesions ranging from fine, mottled infiltrations to soft miliary nodules. The course of the disease is inconstant, but in some of the epidemics that have been reported the acute symptoms have lasted for from four weeks to three months, with a certain amount of disability persisting for a much longer period. The residual pulmonary lesions are sometimes clinically and roentgenographically indistinguishable from those of tuberculosis or carcinoma. The prognosis is excellent in most cases of primary histoplasmosis, but if dissemination occurs it becomes very grave. Treatment varies according to the clinical form of the disease. Asymptomatic patients usually need no treatment; resection has been used in some cases of localized pulmonary disease; and the aromatic diamidines (stilbamidine and propamidine), and ethyl vanillate have been tried in the disseminated form. The good results obtained by the authors with ethyl vanillate in a patient who was acutely ill with primary histoplasmosis suggest that this drug should be given a further trial in cases of severe primary illness.

Systemic Lupus Erythematosus: Review of the Literature and Clinical Analysis of 138 Cases. A. McG. Harvey, L. E. Shulman, P. A. Tumulty and others. Medicine 33:291-437 (Dec.) 1954 [Baltimore].

Increasing familiarity with the varied clinical manifestations of systemic lupus erythematosus, together with improved methods of definitive diagnosis, have led to an altered concept of the character of this disease. It has become apparent that the course is frequently chronic, associated with exacerbations and remissions over a period of many years. The disease is often characterized by recurrent mild illnesses, seemingly unrelated, with prolonged asymptomatic intervals. Even when severe manifestations appear, they may be followed by spontaneous improvement or complete remissions. In some patients, serologic abnormalities antedate by years other evidences of systemic lupus erythematosus, indicating that the disease may remain clinically inactive for indefinite periods of time after the onset. Present knowledge is based largely on retrospective study of cases of full-blown systemic lupus erythematosus, for only recently has it been possible to recognize the disease in its mild or early forms. It is well known that fulminating or fatal illness may occur abruptly or after many years of mild symptoms. However, it remains to be determined whether all cases must necessarily terminate in this fashion. Prolonged observations will be required to establish the course of the disease in the mild cases now being recognized. It is entirely possible that some patients may recover, or that the disease will fail to progress. The possibility cannot be overlooked that even now many mild cases of systemic lupus erythematosus are not recognized for lack of an adequate diagnostic test. It should be emphasized that the negative L. E. cell test does not exclude the presence of this disease. The cause of systemic lupus erythematosus remains obscure, but two features have attracted special attention. One is the almost constant presence of abnormalities of the serum proteins, and the other is the evidence of disease of collagen. The manner in which these phenomena are interrelated and the mechanism of their production have not been elucidated.

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While manifestations of hypersensitivity are common in patients with systemic lupus erythematosus, it has not been established that hypersensitive reactions are of causal significance. Definitive treatment will have to await a better understanding of the pathogenesis of the disease. Striking suppression of the signs and symptoms may be obtained with hormone therapy, but others are unaffected and complications occur frequently. Whether or not life is prolonged by such therapy cannot at this time be accurately ascertained, but the evidence to date is in the affirmative.

Studies on Shingles: Is the Virus Ordinary Chickenpox Virus? R. E. H. Simpson. Lancet **2**:1299-1302 (Dec. 25) 1954 [London, England].

Simpson reasons that if ordinary varicella (chickenpox) and herpes zoster–varicella caught from herpes zoster (shingles) are caused by the same agent, then herpes zoster is a manifestation of varicella virus and patients with herpes zoster excrete the causal organism of varicella in its infectious state. If, on the contrary, herpes zoster–varicella is not caused by ordinary varicella virus, then herpes zoster is not a manifestation of varicella virus. If ordinary varicella and herpes zoster–varicella are caused by the same virus, they will have the same incubation period, serial interval, and infectiousness; and those who have suffered an attack of the one will be refractory to challenge by the other. If they are caused by unrelated agents, there are likely to be dissimilarities of reproductive cycle or of invasive properties, reflected in differences of incubation period, serial interval, and attack-rate; and an attack by one should confer no immunity to the other. The view that they are caused by distinct but related viruses offers an intermediate position. The author reports observations and studies on the relationship between varicella and herpes zoster that were made in connection with outbreaks in the Shetlands. In 1946 Peterson and Black described how, in 1945, herpes zoster in a school teacher in the island of Yell in the Shetlands gaves rise to an outbreak of chickenpox in the pupils. Last March, in the course of correspondence about the 1945 epidemic, Dr. Peterson informed the author that the chain of events appeared to be repeating itself and that cases of chickenpox were occurring in the family of a man with herpes zoster. Later this outbreak extended all over the island. Since the area is well suited for field epidemiology, studies were made in the homes of persons who had had herpes zoster and in those who had had varicella in the 1945 outbreak of herpes zoster–varicella. The evidence collected is strongly in favor of the view that the virus of varicella derived from herpes zoster is identical with the virus of ordinary varicella. The clinical illnesses are indistinguishable; the reproductive cycles of the viruses produce not very different serial intervals; the two viruses have the same order of infectiousness against those who have never had either disease; and each virus confers a protection against the other, which within the limits of these observations appears to be complete. It is concluded that the varicella caught from herpes zoster is due to the same virus as ordinary varicella.

Rheumatic Fever as a Collagen Disease. D. A. Long. Ann. Rheumat. Dis. **13**:324-326 (Dec.) 1954 [London, England].

According to Long, rheumatic fever is typical of the collagen diseases in that lesions of mesenchyma, heart, blood vessels, joints, and serous membranes are frequently associated with hyperglobulinemia, lymphadenopathy, and splenomegaly. Group A hemolytic streptococci play a part in the pathogenesis of rheumatic fever, but there is no simple bacteria-host relationship that can be defined in terms of Koch's postulates. It is the host, not the Streptococcus, that decides the issue, for rheumatic fever develops in only a few patients with hemolytic streptococcic infection. The syndrome occurs when recurrent attacks of hemolytic streptococcic tonsillitis have led to localization of the infection, and a high level of antibodies. The disease is part of what Rantz and others have termed "the post-streptococcal state." This state is always associated with hypersensitivity (of the tuberculin type) to streptococcic allergens. There are indications that a deficiency in sulfur-containing amino acids is in part responsible for increased susceptibility to rheumatic fever. There is the fact that amino acids cannot be stored, and therefore a deficiency is readily induced. Rheumatic fever is less common in farming regions, where the diets provide generous amounts of proteins, than in regions where diets are deficient in proteins. Egg consumption is lower in children in whom rheumatic fever develops than in other children. Powdered egg yolk prevented recurrence of rheumatic fever in underprivileged children in spite of recurrent attacks of hemolytic streptococcic infection. It is noteworthy that hyperglobulinemia and multiple small areas of cardiac necrosis have been described in conditions attributed to a deficiency of animal protein, and that of all sources of protein, egg protein has the highest biological value. Although the body cannot store protein, there are large reserves in tissues that can be withdrawn without impairing vital function. Plasma proteins are readily replaced from tissues; conversely, plasma proteins injected intravenously can supply all the protein requirements of the body. It has been suggested that in the collagen diseases in general, and rheumatic fever in particular, connective tissue provides protein and globulin for the general metabolic pool, this loss being associated with characteristic degenerative changes in mesenchyma. It has been shown recently that gamma globulin provides amino acids for incorporation into liver cells. It is possible that under conditions of protein deficiency hyperglobulinemia represents a compensatory phenomenon. Hyperinsulinism increases, and hypoinsulinism decreases, susceptibility. Cortisone decreases susceptibility. Ascorbic acid requirements are increased. The common factor relating hypersensitivity to these nutritional and hormonal agents is the metabolism of sulfur-containing amino acids and of glutathione. To the criticism that these connections are too complex, the author replies, what simple hypothesis will unite bacterial, allergic, nutritional, and hormonal hypotheses? By considering a single facet of the problem and ignoring the rest, a simple hypothesis can be produced, but this is seeking simplicity where none exists. Rheumatic fever, though complex, is the collagen disease of which most is known. The author has selected clues that can be followed and that may lead to a fuller understanding of the group as a whole.

Modern Ideas Concerning the Prophylaxis of Acute Rheumatic Fever. A. Ravina. Presse méd. **63**:3-4 (Jan. 1) 1955 (In French) [Paris, France].

The successful prophylaxis of rheumatic fever depends on the elimination of the hemolytic streptococci from the nose and throat. Prevention of acute streptococcic infections would result in the virtual disappearance of the disease: fresh cases would not develop and there would be few, if any, recurrences. Various American authors found that penicillin was effective in eliminating hemolytic streptococci when given orally in doses of 800,000 units for seven consecutive days a month during all or part of the year; this method of treatment, however, as well as one in which daily injections of penicillin are given during the first week of each month, involves certain practical difficulties and inconveniences that can be largely overcome by the use of long-acting penicillin. A single monthly injection of 1,200,000 units of benzathine penicillin G in a volume of 2 cc. given to 96 American children who had previously had an attack of rheumatic fever proved capable of assuring an appreciable level of penicillin in the blood for a period of about 28 days. No clinical recurrence of the disease was seen in any of the children during the 14 months this method was under trial, and there were only two somewhat doubtful instances of allergic reaction. The introduction of long-acting penicillin, therefore, constitutes a distinct advance in the prophylaxis of rheumatic fever and its systematic use should bring about a substantial reduction in both the frequency and the severity of this condition in the future.

Role of Various Surgical Operations in the History of Patients with Rheumatoid Arthritis. L. Kalliomäki. Ann. Rheumat. Dis. **13**:341-343 (Dec.) 1954 [London, England].

Although the etiology of rheumatoid arthritis still remains unexplained, a number of external circumstances seem to act as precipitating factors at times. Kalliomäki investigated the role of certain surgical operations in the history of 187 female patients with rheumatoid arthritis. Hysterectomy and/or oophorectomy had been performed in 10 of these women, thyroidectomy also in 10, tonsillectomy in 9, appendectomy in 5, and cholecystectomy in 3. In two cases of thyroidectomy the onset of the rheu-

matoid arthritis was evidently related to the surgical operation. In two other cases an exacerbation of the joint disease occurred immediately after the thyroidectomy. No correlation in time was observed between the other operations studied and the onset or course of rheumatoid arthritis. Patients with rheumatoid arthritis should be subjected to thyroidectomy only if the operation is absolutely necessary.

Clinical Symptoms of Cancer of Esophagus with Particular Reference to the Initial Symptoms. G. Mazzoni. Policlinico (sez. prat.) **61:**1492-1499 (Nov. 8) 1954 (In Italian) [Rome, Italy].

Mazzoni studied 58 patients with cancer of the esophagus who were admitted to the Institute of Surgical Pathology at the University of Rome during the last four years. The neoplasm was found in the cervical section of the esophagus in 7 patients, in the thoracic section in 31, and in the abdominal section in 20. Most of the patients, 51 of whom were males, were between the ages of 55 and 60 years. The onset of the symptoms varied in these patients, and it depended on the location of the neoplasm in the esophagus. They appeared earlier in those patients in whom the neoplasm was found in the cardial area. This seems to offer an explanation for the fact that many patients in whom the neoplasm involves the thoracic or cervical portion of the esophagus seek help when the cancer is already at such an advanced stage that a radical intervention is contraindicated. Also, a cancer in the cervical and thoracic areas of the esophagus spreads mainly in a longitudinal direction, whereas one in the gastroesophageal area develops almost always in a circular direction, and therefore stenotic manifestations appear quite early. Dysphagia, which was by far the commonest symptom, was present in 90% of these patients. It was observed in all those in whom the neoplasm involved the gastroesophageal area, in 90% of those in whom it involved the thoracic, and in 85% of those in whom it involved the cervical area of the esophagus. A retrosternal pain was found in 48% of the patients, salivation in 35%, and regurgitation of a whitish fluid during sleep in 40%. Other symptoms were a fetid breath in 7%; dysphonia in 15.4%; and hiccup, which in some instances appeared even before the dysphagia, in 6.1%. General symptoms, such as asthenia, loss or lack of appetite, loss of weight, and at times fever, were present in 87%. Hypochromic anemia was observed in all the patients and was attributed to continuous microscopic hemorrhages—blood was always found in the feces of these patients—and also to a decreased supply of iron with the food because of the difficulty of these patients in ingesting it. As to the sequence in the onset of these symptoms, dysphagia was the earliest in only 64%. In the remaining patients it appeared about three months after the onset of other signs, which were not considered possible indications of the presence of a neoplasm of the esophagus, thus delaying the correct diagnosis in 36% of the patients. Because these "small signs" may lead to an early diagnosis of cancer of the esophagus they should be evaluated in their true light with esophagoscopy and roentgenography, taking into consideration the age of the patient.

Treatment of Acute Barbiturate Poisoning. N. Michael and C. L. Baker. Ohio M. J. **50:**1029-1031 (Nov.) 1954 [Columbus, Ohio].

Fifteen patients with acute barbiturate poisoning were treated with the Reiter electrostimulator. Of this group, seven were considered to be in serious condition. In general the stomach was washed routinely if the patient's condition permitted. Persons in serious condition were taken directly to their rooms in the hospital, where a rubber airway was placed in the mouth and electrostimulation begun. This undirectional electric diencephalic stimulation causes elevation of blood pressure, increased depth of respiration, and improvement of the pulse. It is the authors' opinion that the electrostimulator maintains life, thus allowing the body to destroy the drug. Intubation was done in some patients in whom the airway did not insure free passage of air in and out of the lungs. Oxygen was available and was used whenever the breathing seemed shallow and the patient was cyanotic. Large doses of metrazol were also available. A doctor or nurse instructed in the use of the electrostimulator was in constant attendance. Of the 15 patients, one died and the others made complete recoveries. Five cases are reported in detail. None of the patients treated in this manner had toxic reactions. On awakening they were cooperative and talked frankly and coherently. Most patients could have been discharged from the hospital within 24 hours after termination of coma. This was in marked contrast to the course of persons treated by other means. Such patients became delirious, restless, noisy, belligerent, and difficult to control. Besides constant attendance, restraints were necessary for a period of five or more days, depending on the individual case. In some cases electrostimulation was used mainly to prevent toxic reactions. In one case it was used to help terminate a toxic reaction, with good results. None of the patients showed any brain damage, with the possible exception of the one who died, even though some were in prolonged coma. It is concluded that, in the treatment of acute barbiturate poisoning, the use of the electrostimulator together with judicious use of analeptics and adequate airway is superior to all other forms of treatment.

Scurvy—A Rare Disease? T. J. Thomson. Glasgow M. J. **35:**363-365 (Dec.) 1955 [Glasgow, Scotland].

A survey of admissions to a general hospital in Glasgow during the past 15 years revealed 100 cases of florid scurvy. There were only six women in the series of 100 cases. Fifty-two of the 58 patients, whose records gave details of the domestic circumstances, lived alone or in lodging houses and did their own cooking. Adequate clinical details were available for 82 of the patients. Eighty of these were found to have signs in the lower limbs—sheet hemorrhages or widespread subcutaneous extravasation of blood, either spontaneous or following minor trauma. This striking physical sign is almost invariably present in ambulant subjects. Sixty-six records included reports on blood examination, and these showed that 82% of the patients had moderate or severe anemia. Not all these cases were correctly diagnosed by the doctors who sent the patients to hospital. The scorbutic lesions were most commonly confused with varicose veins, phlebothrombosis, congestive cardiac failure, osteoarthritis (when suffusion of blood had occurred into or around a joint), and senility. Recovery was complete in 95 patients. The five deaths were attributed to myocardial infarction, pneumonia, hemorrhage from a chronic duodenal ulcer, and inanition. Scurvy is a preventable disease; however, a small proportion of apparently normal people grow indifferent to the simplest dietetic precautions. The author feels that for every case of florid scurvy that comes under medical care there are almost certainly several minor ones that are never seen by the doctor; and it may well be that subclinical scurvy causes a good deal of vague general ill-health wrongly attributed to "old age."

The Effect of Detergent on Intestinal Digestion. B. Fuchs and F. J. Ingelfinger. Gastroenterology **27:**802-810 (Dec.) 1954 [Baltimore].

Detergents are widely employed for washing eating utensils and for cleaning containers used in the preparation, distribution, and consumption of food. Small amounts of these substances must therefore be ingested daily by many people. Much larger doses of anionic detergents have been given to patients with peptic ulcer. The present study was undertaken to determine the effect of a typical anionic detergent, sodium lauryl sulfate, on intestinal digestion and absorption in human subjects. The in vitro effect of increasing concentrations of sodium lauryl sulfate was investigated on pancreatic amylase, lipase, and trypsin, obtained directly from the human duodenum following pancreatic stimulation with secretin. These in vitro experiments showed that sodium lauryl sulfate produces a marked inhibition of pancreatic amylase, lipase, and trypsin. The in vivo effects of sodium lauryl sulfate on the digestion and absorption of starch, lipid, and protein were studied by duplicate tolerance tests with and without detergent. Carbohydrate, in the form of boiled rice, was given intraduodenally, and the blood glucose levels were measured. Natural vitamin A ester was used as the test substance for lipid. Blood levels of glycine following intraduodenal administration of gelatine served as an index of protein digestion. Of the three tolerance tests, the glycine levels were most consistently depressed by adding the detergent. Large amounts of sodium lauryl sulfate depressed the majority of starch and vitamin A curves irregularly. Small quantities of sodium lauryl sul-

fate, even if in high concentration, appeared to enhance the absorption of vitamin A. The results of osmotic fragility tests suggested that no detergent in an active form gains access to the bloodstream following instillation of sodium lauryl sulfate into the duodenum. The results indicate that the chance ingestion of detergent following its household use does not interfere with intestinal absorption of food. Larger amounts of detergent, as used in the treatment of peptic ulcer, may decrease absorption, partly because of enzymatic inhibition and partly because of the detergent's irritant effect on the intestine.

Leprosy of Liver: Clinical Study. L. M. Bechelli. Rev. brasil. leprol. **22**:1-94 (March) 1955 (In Portuguese) [São Paulo, Brazil].

One thousand and thirty-nine patients with leprosy were observed for pathological conditions of the liver in three leprosariums of Brazil. The clinical type of leprosy was lepromatous in 754 cases, neural residual in 31, and neural tuberculous in 228 cases. Hepatomegaly was present in 307 patients; it was painless, marked, and often associated with amyloidosis but rarely with splenomegaly. It was present in nearly all the patients with lepromatous leprosy. The liver on palpation was thickened and dull in a few cases and smooth in the majority of the cases. It was of increased consistency and of smooth surface. Hepatomegaly was very marked in the course of leprotic reactions during which the liver became painful. A diagnosis of leprous hepatomegaly was made by palpating the liver and by the fact that disease developed without fever, ascites, and circulatory disorders. Jaundice may be present if leprous hepatomegaly is complicated by other nonleprotic disease of the liver. Only one-third of the total number of patients with leprous hepatomegaly complained of subjective symptoms, mainly gastric disorders and in rare cases dizziness, anorexia, somnolence, and physical and mental fatigability. The tests for functions of the liver give normal results. Their conversion into abnormal results indicate presence of nonleprotic hepatic disease, discontinuation of antileprous treatment, and administration of treatment for the nonleprotic disease. An autopsy was made in 91 cases. Leprosy of the liver was observed in 66 out of 69 cases of lepromatous leprosy, in 4 out of 5 of neural residual leprosy and in none of the 17 cases of neural tuberculoid leprosy. The histological changes of the liver consisted in periportal lepromatous infiltration, lepromatous induration, amyloidosis, and in extremely rare cases leprous cirrhosis. The leprotic liver was increased in weight in the majority of the cases. Its consistency and characteristics of either thickness or smoothness confirmed those found by clinical examination. Leprotic cirrhosis was observed in only one case. Tuberculosis of the liver was a complication of hepatic leprosy in four cases.

Treatment of Diabetes Mellitus with Insulin Zinc Suspension: Clinical Study Based on 479 Cases. K. J. Gurling, J. A. Robertson, H. Whittaker and others. Brit. M. J. **1**:71-74 (Jan. 8) 1955 [London, England].

The degree of control achieved with insulin zinc suspension in 479 patients seen in the Diabetic Department of King's College Hospital was assessed both objectively and subjectively, although the value to be attached to the subjective factors, i. e., the patient's opinion concerning his well-being and freedom from hypoglycemia and diabetic symptoms as compared with his condition either before any form of insulin was started or on his previous regimen, is limited, because patients are apt to be biased in their attitude towards any new form of therapy. Three objective factors—the degree of night control (A), day control (B), and alterations in weight (C)—were considered in assessing absolute control, and the results were then compared with those previously obtained over a similar period with other forms of insulin. Night control was regarded as good when on at least 75% of examinations the early morning Benedict's test was blue or green (0.5%; one plus). Day control was accepted as satisfactory if the capillary blood sugar level was under 200 mg. per 100 ml. (Folin and Wu). Changes in weight were not considered significant unless they amounted to more than ±2 lb. (0.9 kg.). Control was considered excellent (ABC) when both night control and day control were good and the weight remained stationary or was increased, but, since in many patients a slight loss of weight is desirable, those in the AB and ABC classifications were grouped together and the control for the combined group was described as good. Otherwise, control was assessed as fair if only one or two of the criteria were satisfied and poor when none were met satisfactorily. Failure with insulin zinc suspension occurred in only 32 patients (7% of the entire series). Improvement, on the other hand, was seen in 31% of adults and 37% of children previously treated with insulin in other forms. Some increase in insulin dosage and changes in diet are usually necessary with insulin zinc suspension, and no patient should be changed over to it without adequate supervision. The results obtained by the authors in these patients showed that insulin zinc suspension is a reliable preparation permitting adequate control of many diabetics with one injection a day; further experience, however, has convinced them that there is a recognizable group of patients in whom it fails to control hypoglycemia and prevent ketosis. Patients in this group are relatively insensitive to all the long-acting insulin preparations and cannot be successfully treated without the use of soluble insulin.

Alkaloid of Rauwolfia Serpentina Benth (Reserpine) in Treatment of Arterial Hypertension. S. Borsari and S. Boschi. Minerva med. **45**:1521-1525 (Dec. 8) 1954 (In Italian) [Turin, Italy].

Reserpine was given orally in daily doses of 0.5 to 1 mg. to 48 patients, 27 to 76 years of age, with arterial hypertension. This was essential in 24, arteriosclerotic in 11, renal in 2, and of dubious origin in 11. Seventeen of the patients were hospitalized during the treatment, which was continued for from a minimum of 10 days to a maximum of 114 days. The results were considered excellent when a definite and constant drop of the hypertension and improvement in the objective and subjective symptoms were obtained. They were considered good when the drop in hypertension was moderate and constant, or marked but not stable, and the symptoms were improved; mediocre when there were only slight changes in the initial values and the symptoms remained unchanged; and negative when there were no changes or only slight ones in the hypertension with a quick return to the initial values and the symptoms were not influenced. The therapy was favorable in 50% of the patients, with the greatest percentage of good effects in the patients with arteriosclerotic and essential hypertension. The results were excellent in 11 patients, good in 13, mediocre in 11, and negative in 13. Besides its hypotensive effect the drug had also a marked sedative effect. Anxiety subsided in the patients, who became more tranquil and serene and were able to sleep at night. Because headache, palpitation of the heart, and paresthesia disappeared, they also experienced a notable improvement even when the arterial pressure was not or only slightly influenced. In some patients a persistent constipation was overcome during the treatment. The side-effects (drowsiness) were not marked and subsided in from one to three weeks. Allergic reactions to the drug were seen in two patients only. Toxic effects of Reserpine on diuresis or the various organs were not observed.

Manganese Poisoning. R. Peñalver. Indust. Med. **24**:1-7 (Jan.) 1955 [Chicago].

According to Peñalver much of the manganese used in the steel and other metallurgical industries in the United States is imported from Cuba. The author describes manganese poisoning as observed in the manganese mines in Cuba and cites data from literature on manganese poisoning. The respiratory tract is the most important route of entrance. Manganese has a predilection for certain nerve cells at the base of the brain and the upper portion of the spinal cord. The first manifestations of manganese intoxication are cephalalgia; sleep disturbances in the form of somnolence, insomnia, or restless sleep; sensitivity of the muscles; spasms in the legs and arthralgia; and the gait is usually spastic. Psychomotor irritability, euphoria, absentmindedness, mental confusion, aggressiveness, and hallucination are some of the psychological manifestations. Speech disturbances, such as inability to raise the voice above a whisper, monotonous speech, and disappearance of pauses between words, impulsive laughing, mask-like or wooden facial expres-

sion, tremors, twitching fingers, and disturbances in handwriting have been noted. Impotence was one of the most common manifestations in the cases observed by Peñalver. The results of studies on the blood, urine, and cerebrospinal fluid, of liver biopsies and functions tests, and of encephalographic tests are discussed. As to prognosis, in patients with neurological disturbances the evolution is generally progressive, even though there is no further exposure to manganese. While there may be partial recovery in a few cases, some progress to paralysis, while others remain stationary for long periods. Some workers who are apparently healthy when they leave the mines may show neurological disorders three or four months later. Various treatments have been tried, such as vitamin B_1, Dimercaprol (BAL), and calcium ethylenediaminetetraacetic acid (CaEDTA). At present preventive measures, particularly the control of manganese dust, and personal hygiene (baths and frequent changes of work clothes), proper diets, and quarterly medical examinations are of greatest importance.

The Familial Occurrence of Hypertension and Coronary Artery Disease, with Observations Concerning Obesity and Diabetes. C. B. Thomas and B. H. Cohen. Ann. Int. Med. **42**:90-127 (Jan.) 1955 [Lancaster, Pa.].

The prevalence of hypertension, coronary artery disease, obesity, and diabetes among the parents, grandparents, uncles, and aunts of 266 medical students at Johns Hopkins University was ascertained. At a mean age of 55 years, 12% of parents had hypertension and 5.5% had coronary artery disease. Sixteen per cent of parents had hypertension and/or coronary disease, while 30.7% of grandparents were known to be similarly affected. The incidence rates of these disorders among the parental siblings were slightly lower than the corresponding rates for parents. The incidence of hypertension tended to be higher among women than among men in comparable groups. Coronary artery disease occurred more often among men than among women; this difference was more pronounced in the parents' generation. Of the parents, 12.2% were obese, while 9.3% of the grandparents were so affected. Diabetes was the least prevalent disorder, affecting 2.4% of the parents, with an incidence rate of 4.1% among the grandparents. In the search for evidence of causal interrelationships among the four diseases studied, it was found that combinations of two or more disorders affecting the same individual occurred more frequently among both parents and grandparents than might be expected from chance alone. The degrees of association were particularly high between hypertension and coronary disease and between hypertension and obesity. Comparison of the incidence of other disorders in affected and in nonaffected parents or grandparents again showed significant differences, pointing to the fact that hypertensive persons have more coronary artery disease and more obesity than normotensive persons. A study of the incidence of the four disorders in siblings of affected and nonaffected parents showed that: 1. Hypertension was three times as frequent among siblings of hypertensive persons as among siblings of normotensive persons. 2. Coronary artery disease was nearly four times as prevalent among siblings of persons with coronary disease as among siblings of persons without it. 3. The siblings of obese persons had four times as much obesity as the siblings of nonobese persons. 4. Diabetes was eight times as common among siblings of diabetic persons as among the siblings of nondiabetic persons. The incidences of the various disorders in two successive generations were analyzed by comparing their prevalence among the offspring of matings in which both, one, or neither of the parents was affected. In general, there was a distinct gradation among the offspring of these three types of matings, with the highest incidence of disease among the offspring of two affected parents and the lowest among the offspring of two unaffected parents.

Sleep Therapy in Treatment of Status Asthmaticus. R. Gallini. Sett. med. **42**:582-585 (Nov. 15) 1954 (In Italian) [Florence, Italy].

Prolonged sleep was used to treat five patients with bronchial asthma of long standing in severe status asthmaticus, in whom various therapies, including administration of cortisone and slow phleboclysis of aminophylline, had been of little or no benefit. To mitigate the severe dyspnea all these patients had needed from three to seven intramuscular injections of epinephrine each day. Before sleep was induced, the administration of all drugs was suspended, and during this treatment the patients were given, besides amytal, penicillin and oxygen by inhalation. Sleep was induced slowly with amytal and was maintained from 18 to 20 hours each day. The patients were studied for about three weeks, but the actual treatment lasted only 14 to 15 days because it took two to three days to induce sleep and 5 to 6 to interrupt it gradually. The treatment brought about a quick and marked arrest of the status asthmaticus and a temporary disappearance of the asthma. Anxiety, dyspnea, cyanosis, and pulse rate decreased, and the epinephrine injections were reduced and in some instances even suspended. At the end of the treatment the patients were clinically cured. The treatment was tolerated well by all the patients. These were followed from 20 days to one month at the clinic, and during this time no asthmatic attacks occurred, even though no drug was administered. Isolated attacks recurred several months later, but status asthmaticus did not reappear. One year later two patients returned and volunteered to undergo a second course of treatment hoping to obtain a further improvement. For various reasons this second course was not as successful as the first had been. A follow-up three years after the first treatment indicated that asthma was present in three patients, but it could be overcome with the common drugs. Status asthmaticus was not present in any of them. Gallini attributes the good results obtained not only to the cortical and subcortical inhibiting action of sleep but also to its direct or indirect action on the dysergic phenomena of the bronchial mucosa. The results obtained were qualitatively comparable to those that are generally brought about by cortisone and corticotropin in patients with asthma. In these patients, however, they were more marked because the hormone therapy had failed.

Clinical Studies on Action of Serpasil. O. Conte and M. Porcelli. Sett. med. **42**:588-600 (Nov. 15) 1954 (In Italian) [Florence, Italy].

The good hypotensive effects of Serpasil in four patients with renal and eight with essential hypertension are reported. The drug was given orally in doses of two 0.5 mg. tablets daily for four days and of three such tablets daily thereafter. The arterial pressure, subjective symptoms, and pulse and breathing rate were studied each day. After 12 days of treatment, the fundus oculi, the basal metabolism, the electrocardiograms, and the blood and urine were studied, and the values were compared with those obtained before the therapy was instituted. The arterial pressure dropped in all the patients. The fall was abrupt in six, and in these the new values fluctuated in the post-treatment period, whereas in the other six in whom the drop was gradual the values remained constant. These values were still present four months after the treatment was discontinued. The drug had a general sedative effect on all the patients, in whom the headache and vertigo were also improved. Some patients experienced uncontrollable drowsiness and a need for much sleep. Four who had suffered insomnia found the drug a good soporific. Miosis was observed in all the patients, bradycardia in nine. No change occurred in the fundus oculi, and the drug caused neither hypothermia nor hyperperistalsis. The blood and urine tests did not reveal damage of the drug on the hemopoietic organs and the renal function.

Prolonged Treatment of Severe Asthma with Cortisone in Tablets. J. Turiaf, P. Marland; P. Blanchon and Y. Jeanjean. J. franc. med. et chir. thor. **8**:592-616 (No. 6) 1954 (In French) [Paris, France].

Of 55 patients with severe continuous asthma with dyspnea treated with cortisone tablets over a period of two years, 22 were chosen to be reported on because they had had this treatment for a period of at least three months uninterruptedly. The maximum period of uninterrupted treatment among this group of patients was 24 months. Long-standing asthma with continuous dyspnea, regardless of the length of past duration or the age of the patient, is one of the clearest indications for ambulatory cortisone therapy. The other principal form of severe asthma

requiring cortisone treatment is that accompanied by prolonged and easily relapsing states of asthmatic disease. Only patients with asthma that does not yield to the usual forms of therapy are to be treated with cortisone. The action of the hormone is manifested rapidly and emphatically. In about one week freedom of breathing is noted, together with suppression of cough and reduction of expectoration. The proper maintenance dose is the smallest that will relieve the patient's symptoms. This is usually between 50 and 75 mg. per day taken four times in every 24 hours for the first five days of every week. The patients must be on a low sodium, low chloride diet and receive 1.5 to 2 gm. daily of potassium chloride. Once a week they are given an intramuscular injection of 40 to 50 mg. of testosterone. They must be under careful surveillance even though they are outpatients, because this treatment has considerable risk. This treatment is perfectly acceptable for continuation over a period of months and probably years. Only one accident occurred among the 55 patients treated; cavitary tuberculosis appeared during the 18th month of therapy. Otherwise, the method was eminently successful, restoring all of the patients back to normal life.

Chronic Bronchitis: An Attempt to Control Chronic Infection with Hemophilus Influenzae by Aerosol Therapy. K. Knox, P. C. Elmes and C. M. Fletcher. Lancet **1**:120-122 (Jan. 15) 1955 [London, England].

Knox and co-workers tried local therapy with streptomycin and penicillin in patients with chronic Hemophilus influenzae infections to see whether such therapy could be applied effectively for long periods without serious complications, such as sensitivity to the drugs and a serious proliferation of insensitive organisms. The method was tried in three inpatients, who had been admitted with acute exacerbations of their chronic bronchitis and were found to have a predominant growth of H. influenzae in their sputum. The six outpatients were not acutely ill when treatment was started but were less well than they had been in the summer. All were known to have had a predominant infection with H. influenzae for at least a month, some for more than a year, and they had been under observation during the preceding winter. None had received chemotherapy within a month of the start of the trial. The dose of penicillin G and streptomycin sulfate was dissolved in 1.5 ml. of 0.5% isoprenaline sulfate. This was dispensed in rubber-sealed bottles containing a week's supply and retained its potency at room temperature over this period. The patients measured out the dose with a 2 ml. syringe and used an electrically driven plastic inhaler with a face mask. They were instructed to gargle and to wash their faces and hands after each treatment to diminish the risk of skin sensitization. The inhalation usually took from 15 to 20 minutes. H. influenzae was eliminated from the sputum of three of the patients. In the others H. influenzae persisted in the sputum and they had winter exacerbations of their bronchitis. The authors conclude that their method of administering penicillin and streptomycin as an aerosol cannot be relied on to control bronchial infection by H. influenzae. Furthermore, even the one patient in whom the infection was controlled for as long as six months relapsed immediately after the treatment was stopped. The reason for the failure of the method in five out of six patients is not clear, because the persistent organisms retained their original sensitivity to penicillin and streptomycin. Perhaps the uneven distribution of an inhaled aerosol in emphysematous patients permits foci of infection to persist in parts of the lung to which the aerosol does not penetrate.

Jackson's Bronchial Adenoma. M. Chauvet and R. Lasserre. Schweiz. med. Wchnschr. **85**:49-53 (Jan. 15) 1955 (In French) [Basel, Switzerland].

Two cases of Jackson's bronchial adenoma in a 33-year-old man and in a 48-year-old woman are reported that illustrate the authors' opinion that the symptomatology of these tumors is dominated by two major facts, i. e., hemoptysis depending on the highly vascularized connective stroma of the tumor, and bronchopulmonary suppuration, which is attributable to the localization of the tumor in the large bronchi and to its slow course. In the case of the man, the patient had pulmonary symptoms since he was 19 years old. They were characteristic of bronchial irritation with "congestive episodes," and there was recurrent hemoptysis associated with more or less profuse bleeding, while from the onset of the disease roentgenograms showed dense and homogenous shadows in the right lower lobe. The patient was hospitalized several times for prolonged periods totaling more than two years, in the course of which successive diagnoses were made of bronchopneumonia, pulmonary tuberculosis, dry hemoptysic bronchiectasis, and asthma. Bronchoscopy established the presence of an adenoma of the right lower lobe. Right middle and lower lobectomy was performed, and the patient recovered completely from his disease of 14 years' duration. The second case history was typical of a patient with the bronchopulmonary suppuration syndrome. In the course of five years the woman had eight acute attacks of pulmonary inflammation, always localized at the base of the lower left lobe; successive diagnoses were made of febrile pleurisy, pneumonia, pleuropneumonia, bronchopneumonia, and even postpleuritic tuberculosis. Bronchoscopy revealed an adenoma of the left lower lobe, which was removed. The patient was cured. The transitory inflammatory attacks depended on a permanent anatomic obstruction causing temporary congestion of the mucosa, since the tumor was relatively mobile in the bronchial lumen. On the contrary, in the case of the man, the tumor growth resulted in complete obstruction of the bronchial lumen. Jackson's bronchial adenoma represents a well-determined nosological entity, which is probably identical with that of the mixed tumors of the salivary glands, with which it shares the microscopic polymorphism and the highly peculiar local course. Clinical diagnosis is based essentially on history dominated by hemoptysis and the syndrome of bronchopulmonary suppuration, and on bronchoscopic findings, which nearly always can establish the diagnosis. As a general rule, surgical treatment is preferred in the form of partial resection or occasionally of bronchotomy combined with plastic operation. Local treatment by endobronchial electrocoagulation should be reserved for cases in which surgical intervention is contraindicated on general grounds or in which the functional condition makes resection impossible.

SURGERY

The Brock Operation for Pulmonary Stenosis: Review of 39 Cases. N. A. Antonius, A. D. Crecca, H. A. Murray and others. J. Pediat. **46**:54-66 (Jan.) 1955 [St. Louis].

Antonius and associates present observations on 39 patients with pulmonary stenosis, in whom the Brock procedure was employed. This operation differs from the extracardiac shunt operations of Blalock or of Potts, by directly attacking the stenotic pulmonary valve or infundibulum. The ages of the 39 patients ranged from 3 months to 36 years; 11 were less than 6 years old and 2 were over 25 years of age. In 27 of the patients the pulmonary stenosis was associated with an interventricular septal defect and overriding of the aorta (tetralogy of Fallot). There were 11 cases of pulmonary stenosis with intact ventricular septum and coexistent interauricular communications of varying degree, and one case of pure pulmonary stenosis with intact septums. The diagnosis was established in the majority of patients on the basis of clinical findings and ordinary laboratory procedures. Angiocardiographic and catheterization studies were performed in some cases where the diagnosis was not certain. Of the 10 deaths, 9 were operative deaths, the 10th patient did well for six months and then died of brain abscess. Seven of the nine operative deaths occurred in children less than 6 years of age, and five of these seven belonged to the group with tetralogy of Fallot. The authors feel that the Brock procedure is the only one available for surgical relief of pulmonary stenosis without a ventricular septal defect, whereas in the treatment of the tetralogy of Fallot the surgeon has a choice of either the Brock or Blalock procedures. The choice is influenced by the following factors: the presence of valvular or infundibular stenosis, whether the infundibular stenosis is due to a fibrous septum or a long, narrow, muscular tract; the presence or absence of a pulmonary artery; the size of the pulmonary artery; and the degree of overriding of the aorta. Unfortunately, these questions cannot be answered with sufficient accuracy with the present methods of investigation, and, therefore, to a great extent the choice of operation is empirical. The mortality of the Brock procedure is

high in the tetralogy of Fallot in children below the age of 6 years. Since in this group a severe form of infundibular stenosis is likely to be present, the Blalock procedure should be done. In the older age group of the tetralogy of Fallot, there is more likelihood that the stenosis will be valvular or that an infundibular stenosis will be less severe. In this group the mortality rate of the Brock procedure is low and the results are excellent. In this group, therefore, the Brock procedure is the one of choice. In the presence of overriding of the aorta of more than 50%, neither procedure is feasible and surgery is contraindicated with the methods available at present.

Mitral Stenosis and Commissurotomy. E. D. Gagnon. Surg., Gynec. & Obst. **100**:83-87 (Jan.) 1955 [Chicago].

Gagnon prefers the term commissurotomy to valvotomy or valvuloplasty, pointing out that surgical enlargement of a mitral stenosis must have as its aim the separation of the fused commissures. He presents the surgical results obtained in 100 cases. Although the classification of the American Heart Association is far from ideal when studying surgical indication or postoperative results, the 100 cases are nevertheless grouped according to it. However, a different classification, aiming to group the patients objectively on a basis of numerical factors, is being worked out. The author does not recommend surgery in stage 1, that is, in the asymptomatic stage, believing that the surgical risk is not justified in a patient without symptoms. Patients in stage 2, who present a pure mitral stenosis with some symptoms mostly on exercise, are ideally suited for surgery. Fifty-six of Gagnon's patients were in this stage. The largest percentage of excellent results and the lowest mortality rate was found in this group. The patients in stage 3 present most often subacute pulmonary edema with occasional paroxysmal attacks and progressive cardiac decompensation. Nevertheless, with adequate preparation, the results are still sufficiently good to justify proposing the operation. The patients in stage 4 are the problem cases. These patients are often cardiac invalids with right ventricular failure, sometimes with definite signs of myocardial failure to a degree that would place them in a "bad risk" category, even for more minor surgical procedures. The author does not deliberately suggest operating on this kind of patient, and in the 11 cases in which it was done the patients were warned of the risk involved. Discussing the technical aspects of the operation, the author suggests that the patient's tolerance to cerebral anoxia should be increased before operation by daily carotid compressions. They are not operated upon unless they can stand manual bilateral compressions of the carotid arteries for periods of five minutes without symptoms. As regards the use of the instrumental or digital technique of commissurotomy, the author found that digital fracture is sufficient in 43% of cases. The use of the commissurotomy knife seems to be reserved most often to complete a fracture. The narrow point of origin of the auricular appendage can be dilated by steady pressure with the finger without fear of atrial tear. It does not appear necessary to obtain a very large opening of the mitral valve in order to secure both subjective and objective relief and to reduce the intra-atrial pressures by 50%.

Hypothermia in Heart Surgery. E. Ciocatto. Riforma med. **68**:1269-1270 (Nov. 13) 1954 (In Italian) [Naples, Italy].

Generalized hypothermia has made it possible completely to stop the blood circulation and to carry out with relative ease difficult operations on the bloodless heart and especially on its valves. This passive, external procedure to which the organism is subjected is carried out mainly with physical means that influence the thermotaxic and thermogenetic mechanisms. According to Ciocatto, it is best to lower the temperature to 26 C (79 F) even though some American authors have reported good results at 22 C (72 F). After the usual preparation of the patient and administration of oxygen through a nose tube, a synthetic antihistamine, which also induces sleep, and then a ganglioplegic are administered, the latter in a dose of 0.25 mg. per kilogram of body weight. This induces the onset of a vasomotor paralysis and therefore a greater amount of blood comes into contact with the refrigerating milieu, thus facilitating the lowering of the temperature. A "refrigerating suit" is then put on the patient, and by this the internal temperature is lowered quickly—in about 30 minutes—to 28 C (82 F). Around this point (26 C) there is a total loss of consciousness and the reflexes are abolished, owing also to the action of the ganglioplegic. Curare is then administered, tracheal intubation is carried out, and the operation is performed. Ciocatto states that oxygen should be administered during the entire period of hypothermia, because in such a condition the oxyhemoglobin dissociation curve is changed markedly, owing to the difficulty with which oxygen is released, so that the tissues must use that which is free in the plasma. Once the operation is concluded, reheating must be carried out rapidly, reaching a temperature of 35 C (95 F) within 30 minutes. The author has operated on 96 neurosurgical patients and 65 heart patients in whom generalized hypothermia was induced. There were four deaths in the second group, but these were not necessarily due to the hypothermia. As to contraindications to this procedure, Ciocatto states that there are none, this method being especially indicated for patients whose condition is extremely poor. He never observed functional loss on the part of the nervous system in his patients. This was also true of those in whom the circulation was interrupted for more than 10 minutes.

Round Pulmonary Foci and Their Practical Importance. A. Brunner. Deutsche med. Wchnschr. **80**:14-16 (Jan. 7) 1955 (In German) [Stuttgart, Germany].

Round pulmonary foci are pathological anatomic changes that appear as solitary, circular, sharply circumscribed shadows in the roentgenogram. The diagnosis of tuberculoma may be confirmed by other definite signs of a specific disease of the lung or even by the demonstration of Mycobacterium tuberculosis in the sputum. The tuberculous origin is definite if the roentgen picture of the round focus shows the characteristic stratified structure, circumscribed calcifications, or a disintegration center. An illustrative case is reported in a 44-year-old man who at the age of 33 had tuberculous infiltration in the left upper lobe, with an infraclavicular caseated lesion the size of a hazelnut, which was partially calcified. As a result of high altitude treatment his work capacity was fully restored for 10 years. After an acute bronchitis, tubercle bacilli were again found in the sputum and tomographic examination showed definite breaking down of the old caseating focus. Resection of the posterior apical segment of the upper lobe revealed in addition to the expected tuberculoma a circumscribed atelectasis of the apex with numerous small caseating foci. It will never be possible to decide from the clinical aspect of such a case whether the tuberculoma is active; caseating foci with a diameter of about 2 cm. should be resected on principle, since a small, apparently healed caseating focus may suddenly break down with dissemination of bacilli. Limited surgical intervention in the form of wedge or segmental resection will frequently be adequate. Resection of a round pulmonary focus is to be recommended for additional reasons, since the expected tuberculoma may mask a tumor of the lung. Six illustrative cases in three men and three women between the ages of 23 and 65 years are described. Wedge resection, segmental resection, and lobectomy were performed, respectively, in these patients and revealed a neurofibroma in a 23-year-old woman, a lingular chondroma in a 39-year-old man, a lymphosarcoma or plasmocytoma in a 24-year-old man, an adenocarcinoma in a 65-year-old woman and in a 64-year-old man, and a lymphoblastoma in a 60-year-old woman. The removal of a benign tumor in the first two patients showed that the previous disastrous diagnosis of tuberculosis was erroneous, while in the patients with malignant tumors their early detection made a cure possible. Slow growth of the tumor does not warrant definite exclusion of a malignant tumor. The removal of benign lesions is desirable likewise, since as a rule their growth cannot be checked and sooner or later symptoms will develop.

Postoperative Thrombosis of the Aorta Following Coarctectomy: Report of a Case Treated with Intravenous Trypsin. W. A. Niermann and J. E. Bradley. Bull. School Med. Univ. Maryland **40**:5-14 (Jan.) 1955 [Baltimore].

Niermann and Bradley present the case of a girl, aged 7, with coarctation of the aorta of the adult type and an interatrial septal defect proved preoperatively by cardiac catheterization and angiocardiography, who underwent resection of the co-

arctation and end-to-end anastomosis of the aorta. The immediate postoperative result was good until the 12th day after operation. At this time there was an increase in the brachial blood pressure concomitant with the disappearance of femoral pulsations and blood pressure. It was thought that a thrombus had formed at the operative site of anastomosis in the aorta, causing partial to complete occlusion of the vessel. Symptoms and signs of cardiac decompensation did not occur because of the excellent collateral circulation that was present preoperatively and the relative slowness of the process of thrombus formation. Trypsin was administered intravenously for seven days (total of 900,000 units) followed by bishydroxycoumarin (Dicumarol). There was a decrease in the brachial blood pressure, the femoral pulsations returned, and femoral blood pressure was again obtained. The patient was discharged from the hospital and has continued to do well for 18 months following operation. It is assumed that the enzymatic fibrinolytic and thrombolytic effect of the intravenously administered trypsin resulted in dissolution of a thrombus at the operative site with a reestablishment of the aortic circulation.

An Alternating Consecutive Study of Vagotomy and Emptying Procedure Versus Subtotal Gastrectomy in the Treatment of Duodenal Ulcer: Report of 112 Cases. J. E. Hamilton, A. M. Berg, D. W. Kinnaird and E. Duncan. J. Kentucky M. A. **53**:38-45 (Jan.) 1955 [Louisville, Ky.].

Differences of opinion between the advocates of subtotal gastrectomy and those employing vagotomy and an emptying procedure for patients with duodenal ulcer led the authors to institute a comparative study of the two procedures. Patients with marginal ulcers, perforated ulcers, and actively bleeding ulcers were excluded from the study, which began on Jan. 30, 1950, and is still in progress. All other patients subjected to elective surgical treatment for duodenal ulcer are included, regardless of the degree of obstruction, electrolyte imbalance, or recent hemorrhage, but in order to allow an adequate follow-up this report deals only with those treated up to Jan. 30, 1953, or 56 in each group. Vagotomy was combined with pyloroplasty in 42 cases, and with gastroenterostomy in 14, but in this small series no definite superiority can be ascribed to either method. The gastrectomies were performed in the usual manner, with an anastomosis of the Hofmeister type in all but a few cases. Preoperative evaluation of the patients with regard to factors pertaining to the severity of the disease or physical defects that might add to the surgical risk showed that the two groups were essentially similar, except for a higher incidence of previous perforation in the vagotomy group, 23 instances as against 11 in the group subjected to gastrectomy. Analysis of the results obtained failed to show any significant difference between the curative effects of the two procedures; vagotomy, however, possesses three advantages: it is definitely safer; it leaves the patient his stomach; and, if the ulcer recurs, a conservative gastrectomy can be carried out much more safely than further resection for stomal ulcer following subtotal gastrectomy. The fact that the percentage of failures (17.9%) in each group was higher than that commonly reported may be connected to some extent with the patients' service-connected disability pension status; only 33% of those who obtained results classed as good or excellent received the disability allowance for ulcer, while among those with results classed as improved, i. e., still partly incapacitated, or failure, 77% were receiving it.

Acute Intussusception: Review of 200 Cases. J. Kyle. Ulster M. J. **23**:117-123 (Nov. 1) 1954 [Belfast, Ireland].

Kyle bases his review on a study of the records of 200 patients with acute intussusceptions admitted to the Royal Belfast Hospital for Sick Children during the 10 year period of 1943 to 1952. The cases were consecutive and unselected, and occurred in 187 infants and children under 12 years of age. All were treated surgically, except for the three children whose intussusceptions were unintentionally reduced by diagnostic barium enemas. The classical signs and symptoms consist of colicky pain, vomiting, a palpable tumor, and the passage by the rectum of blood resembling red-currant jelly. Unfortunately, all four are not often present together in the first 24 hours, when it is important to make the diagnosis. The passage of blood and mucus per rectum or blood on the examining finger was noted in 158 patients; a tumor was palpable per abdomen in 132. About one-third of the infants showed the "knees up" sign, and some of the children sat up or went into the knee-elbow position during spasms. Most of the patients were operated on in about one hour's time after admission. The operative procedure consisted of simple reduction in 183 cases. Two infants died on the table before reduction could be attempted. The intussusception was found to be irreducible in 12 patients. In one of these cases an ileotransverse colostomy alone was performed, but the child died. Resections were carried out in 11 cases. Nine of these children underwent end-to-end anastomoses, with three survivals; in two cases early in the series a Mickulicz type of resection was performed; both children died. There are three different ways of dealing with the irreducible intussusception—by resection and end-to-end anastomosis, by a Mickulicz type of resection, and by a short-circuiting operation. A modification of the Mickulicz type of resection was described by Jones in 1953. The author feels that some form of a Mickulicz resection is best for irreducible intussusception. Possible causal agents were found at operation on 11 occasions. They consisted of four Meckel's diverticula, two polyps, one enterogenous cyst, one adherent tuberculous gland, a gross malrotation of the intestine, a fibroma, and one lymphosarcoma of the ileum. There were 16 deaths from intussusception. Resections were necessary in 8 of the 16 cases. The benefits of surgery were not denied even to children who appeared moribund. Twelve children experienced recurrences, the interval between attacks varying from five days to 19 months. A one-year-old girl had three separate intussusceptions within three weeks. The 6% recurrence rate in this series was relatively high, other reports recording it to be between 1 and 2%.

Acute Upper Alimentary Tract Ulceration and Hemorrhage Following Neurosurgical Operations. R. A. Davis, N. Wetzel and L. Davis. Surg., Gynec. & Obst. **100**:51-58 (Jan.) 1955 [Chicago].

The investigation by Davis and associates concerns only those patients who were subjected to surgery. An analysis of 7,000 operative and clinical records distributed over the past 30 years revealed 48 examples of acute upper gastrointestinal ulceration or hemorrhage during the postneurosurgical period. In 943 craniotomies, there were 24 instances in which this complication occurred; in 350 suboccipital craniectomies it was found during the postoperative course of 7 patients. Inquiries regarding gastrointestinal tract symptoms were made in all patients prior to surgery, and acute fatal, or nearly fatal, episodes of hematemesis occurred following the neurosurgical operation in all eight patients with preexisting complaints. There were 12 patients who initially had a smooth postoperative course and who would have recovered from the neurosurgical procedure had it not been for massive gastrointestinal tract hemorrhage. Autopsies performed in 24 of 30 deaths revealed ulceration or gastrointestinal hemorrhage in 15 instances. Single or multiple ulcerations at the cardioesophageal junction, stomach, or duodenum, were observed in 9 of the 15 cases. The ulcerations extended through the muscularis mucosae of the involved structure and were characterized by lack of fibrosis and induration, that is, they were acute. There was a single example in which fatal hemorrhage was caused by rupture of esophageal varices; in two other patients, esophageal varices were important associated pathological conditions. In the remaining five cases, there were multiple areas of mucosa erosion of the stomach and esophagus. In the remaining nine autopsies, no gastrointestinal tract disease was demonstrated, although hematemesis was a prominent feature in the postoperative course. There were 18 other patients who survived episodes of hematemesis and subsequently recovered. Fatal hematemesis and ulceration usually occurred during the first 48 hours postoperatively, although there were several instances in which symptoms developed at a later period of six to eight days, with subsequent death. The patients who survived the more severe bouts of gastrointestinal tract hemorrhage, and those who succumbed as a result of it, all had severe shock, anemia, and hyperthermia. There seemed to be no cor-

relation between the histological character of the lesion in the nervous system and the occurrence of the lesions of the gastrointestinal tract. The anatomic extent of the lesions in the central nervous system was large, with most frequent involvement of the frontal lobe. Gastrointestinal complications developed not only after interventions on the brain but also following such procedures as laminectomy, hemilaminectomy, and trigeminal neurectomy. Small destructive hypothalamic lesions were made in a group of 15 cats using the Clarke stereotaxic apparatus. The animals were autopsied at varying intervals from six weeks to six months; the brains were examined by serial section through the hypothalamus. There were five animals with anterior hypothalamic lesions, five cats with tuberous lesions, and another five with posterior hypothalamic lesions. Autopsy of the entire gastrointestinal tract failed to reveal any evidence of either an acute or a chronic type of ulceration. It is suggested that these postneurosurgical ulcerations and hemorrhages of the gastrointestinal tract represent an extreme pathophysiological response to the physical stress of surgery wherever its location.

The Age Factor in the Mortality Rate of Patients Undergoing Surgery of the Biliary Tract. F. Glenn and D. M. Hays. Surg., Gynec. & Obst. **100**:11-18 (Jan.) 1955 [Chicago].

Glenn and Hays analyzed the age factor in the surgical treatment of biliary tract disease in a series of 4,050 patients receiving surgical treatment for such lesions at the New York Hospital of the Cornell Medical Center in New York during the 21 year period ending Sept. 1, 1953. It was found that among patients under 50 years the rate of fatal complications in nonmalignant disease of the biliary tract was 0.65%. Among patients 50 to 64 years old this rate was 2.5%, and among patients over 65 years of age it was 6.7%. For elective surgical procedures the difference in mortality was not significant. Elective biliary tract surgery is tolerated remarkably well by the geriatric patient. The high mortality rate among aged patients occurs following emergency surgery. The complications of acute cholecystitis in the aged patient with degenerative disease are the chief factor in the operative risk. Older patients with acute cholecystitis should receive surgical treatment, but operation should be performed as early as possible in an acute attack before complications such as perforation, stone obstruction, and jaundice develop. The experience of these authors seems to justify the policy of regarding all cholecystitis due to the presence of calculi, whether symptoms are present or not, as a potential hazard and an indication for elective cholecystectomy. Unique aspects of biliary tract disease in the aged include: (1) an increased incidence of acute cholecystitis, (2) an increased incidence of choledocholithiasis with larger and more numerous choledochal calculi, (3) the occurrence of acute processes in the biliary tract with minimal signs and symptoms, and (4) the increased incidence of associated biliary tract neoplasia.

Factors of Vasoconstriction and Vasodilation in Shock. M. Nickerson. J. Michigan M. Soc. **54**:45-49 (Jan.) 1955 [St. Paul].

Nickerson shows that the interaction of various factors in initiating and perpetuating the vicious cycle of circulatory failure referred to as shock is most complex. Reduced effective blood volume and vasoconstriction are key factors in this cycle. Evidence is presented to indicate that excessive vasoconstriction is an important factor in the genesis of shock. Hypotension associated with vasodilatation is usually well tolerated for long periods of time, whereas comparable hypotension associated with vasoconstriction leads to irreversible shock within a few hours. The only procedures that have been found consistently to reduce mortality following hemorrhage or trauma are those that increase the circulating blood volume or reduce vasoconstriction. Preoccupation with hypotension, an obvious and readily measured sign of shock, has led to the frequent use of vasoconstrictors in therapy. These agents are usually effective in raising the blood pressure, but a consideration of the role of vasoconstriction in the evolution of shock indicates that they are more likely to be deleterious than beneficial, and this conclusion is emphasized by the fact that these agents have never been shown to improve the survival rate in any type of shock produced under controlled conditions.

An End Result Study of Spine Fusion for Lumbosacral Disorders Excluding Disk Herniations. E. C. Bragg and J. Woodcock. New York J. Med. **55**:83-87 (Jan. 1) 1955 [New York].

Of 214 clinical patients of the New York Orthopedic Hospital who underwent lumbosacral spine fusions for joint derangement, exclusive of disk herniation, between 1937 and 1945, 100 were followed up for at least five years. End-results were excellent in 67 of these 100 patients, good in 21, fair in 7, poor in 4, and unclassified in one. Occupational results were satisfactory in 95%. Those returning to full heavy work included laborers, machinists, truck drivers, farmers, house painters, and a carpenter. There was a high incidence of lumbosacral structural variations in the patients operated on. Facet variations seemed of little significance. Disk degeneration and thinning are considered to have an important bearing on symptoms. Disk degeneration and symptoms of chronic lumbosacral derangement occur most frequently at the two lowest lumbar joints. This may be chiefly due to postural and anatomic characteristics. Posterior tilting of the sacrum and mobility are constant factors that may localize disk degeneration in the low back. The relation of the nerve roots, disk, and facets seems to be of fundamental importance in producing symptoms. The disk degeneration itself may be more important than the individual structural variations in exaggerating the fundamental anatomic vulnerability of this area. Spine fusion did not seem to harm unduly the proximal joints.

Diaphragmatic Hernia: Report of 83 Cases. C. J. Donald and O. W. Clayton. Am. Surgeon **21**:45-49 (Jan.) 1955 [Atlanta, Ga.].

During the period from 1950 to 1954 Donald and Clayton operated on 83 patients with diaphragmatic hernias. They stress that the symptomatology is determined by the organ or organs that are involved. There are cases in which only the stomach is herniated and those in which other organs are protruded into the thorax. The first group usually is a hiatal hernia and the latter group usually is traumatic in origin. Sixty of the 83 patients treated by the authors had esophageal hiatal hernia. In 5 of these 60 a diagnosis of acute coronary occlusion had been made, and 4 were given a diagnosis of diseased gallbladder. The authors comment on hernias through the foramen of Morgagni, which they observed in four cases. There were nine cases of congenital and nine of traumatic origin. One hernia resulted after a splenectomy in which a thoracoabdominal approach was employed. There was one death in the 60 patients with esophageal hiatal hernia, and two newborn infants with congenital hernias died. All the other patients were cured. The authors emphasize that symptoms of diaphragmatic hernia commonly simulate those of gallbladder disease, stomach disease, and angina pectoris. Patients with symptoms of these diseases, in whom the suspected disease has not been proved, should be carefully examined for diaphragmatic hernia.

Cardiospasm. G. M. Brownrigg. Canad. M. A. J. **72**:104-107 (Jan. 15) 1955 [Toronto, Canada].

Four case histories are given of patients with cardiospasm. They were successfully treated by the author by means of extramucosal myotomy of the cardioesophageal musculature. Relief of symptoms was noted immediately after operation, despite the fact that roentgenographic abnormality persisted. This took the form of esophageal dilatation, which was seen both before and after operation on the roentgenograms, but not at operation. The delay in the passage of barium into the stomach observed preoperatively was no longer present postoperatively. Myotomy appears to be the best treatment for cardiospasm. It is definitive, unlike dilatations of any sort, and has not been reported to produce esophagitis or peptic ulceration, though there is some experimental evidence to the contrary. Cardioplasty procedures that are similar to pyloroplasty do cause these disorders. When performing myotomy, it is advantageous to use a transthoracic division of the esophagocardial muscle fibers, since this provides simultaneous exposure of the gastric cardia and a greater extent of the lower esophagus than can be seen when the abdominal approach is used. Another advantage of the transthoracic route is early detection of resectable neoplastic obstructive lesions.

Mesenteric Vascular Occlusion. W. R. Morris. M. Ann. District of Columbia **24:**12-16 (Jan.) 1955 [Washington, D. C.].

Morris reviews observations on 19 patients with mesenteric vascular occlusion who were observed at Doctor's Hospital in Washington, D. C., during a 13 year period. The histories of two patients who were treated successfully are presented in detail. The author lists as causal factors: heart disease (rheumatic heart disease or auricular fibrillation) and arteriosclerosis; infections that cause thrombophlebitis, such as appendicitis, pelvic abscess, peritonitis, septicemia, or parotitis; hematogenous factors, such as blood dyscrasias, splenic anemia, and polycythemia vera, or trauma to the mesenteric vessels, particularly at the time of an operation; mechanical factors that result in portal stasis, as pressure from intra-abdominal tumors; and thromboangiitis obliterans. The variable character of the symptoms and physical findings often leads to an erroneous diagnosis, such as intestinal obstruction, cholecystitis, or some other condition. Shock is usually more pronounced in mesenteric vascular occlusion than in other abdominal conditions. Physical findings include variable degrees of abdominal tenderness, rigidity, distention, and the absence of peristalsis. In cases in which arteriosclerosis is the main causal factor, the patient may complain of "intermittent intestinal claudication" or "abdominal angina." This aching, gnawing abdominal pain usually comes on one or two hours after meals. The prognosis in mesenteric vascular disease is poor. Emphasis should be placed on the following points: (1) early diagnosis; (2) immediate surgical intervention after a tentative diagnosis is made; (3) rapid and adequate removal of the damaged intestine, unless there is conclusive evidence that it is viable; (4) the use of blood transfusions, possibly intra-arterial transfusions; (5) a postoperative regimen of continuous gastrointestinal decompression and supportive parenteral therapy; (6) immediate heparinization and delayed dicumarol therapy; (7) the use of an antispasmodic agent and antibiotics; and (8) the importance of operation even in apparently hopeless cases. The author hopes that with such a program the mortality rate might be lowered.

Is Total Gastrectomy Justified in Carcinoma of the Stomach? R. Colp and E. E. Jemerin. New York J. Med. **55:**75-82 (Jan. 1) 1955 [New York].

Of 344 patients with carcinoma of the stomach, 157 were admitted to the Mount Sinai Hospital in New York City between 1938 and 1942 and 187 between 1943 and 1947. The significant differences between these two five-year period groups of patients were an increase in resectability from 41 to 52% through technical advance and extension of operative limits and a decrease in mortality from 35 to 20% resulting from the better understanding and control of fluid, protein, electrolyte, blood and vitamin replacement, chemotherapy, and improved anesthesia. Coincidentally there was an improvement in results as evidenced by a comparison of recent and older three and five-year survival rates: in the first five-year group 33% of the patients surviving resection lived for more than three years and 23.8% were alive five years or more, as compared to 42.9% who in the second five-year group survived for more than three years and 27.3% who were alive five years or more. These follow-up statistics corresponded more or less with those reported by other surgeons in that one-quarter to one-third of the resection survivors lived for five years or longer, but when the tumor was confined solely to the stomach, the survival rate was as high as 50%. The question was raised as to whether a further improvement in long-term results would not be obtained by the more frequent or routine use of total gastrectomy even for early limited lesions. A review of the literature showed that although the mortality of total gastrectomy has been much reduced, it remains appreciably higher than that for subtotal resection. It is likely that any increase in survival would be outweighed by the greater death rate from the procedure. Moreover, morbidity and invalidism following total gastrectomy are significant features. Total gastrectomy does not solve the problem of eradicating lymphatic spread beyond the limits of technical accessibility, and this is the condition responsible for most survival failure. A significant improvement in long-term survival will probably depend on earlier diagnosis when the lesion is still relatively confined, permitting the performance of a standardized radical subtotal gastric resection. Total gastrectomy should be reserved for those patients in whom the entire or proximal stomach is involved.

The Saddle-Flap for Surgical Repair of Ischial Decubitus Ulcers. R. M. Campbell and J. M. Converse. Plast. & Reconstruct. Surg. **14:**442-443 (Dec.) 1954 [Baltimore].

Campbell and Converse show that an ischial decubitus ulcer may become an obstacle to the rehabilitation of the paraplegic patient. Conservative treatment for a period of one month is the maximum amount of time allowed for spontaneous healing when the deep ulcer shows no signs of improvement. Excision of the lesion and approximation of the wound edges, which is a surgical compromise, has almost uniformly yielded poor results. The treatment of choice is excision of the ulcer, removal of the sharp protuberance of the ischial tuberosity when present, and flap coverage. A saddle-flap, based medially, is raised from the posteromedial aspect of the thigh below the gluteal fold. Such skin is of good quality, with a thick layer of subcutaneous fat, and is almost never involved in trophic changes, unlike the lateral skin of the thigh and the buttocks, which in many cases is scarred by previous decubiti. The saddle-flap also parallels the direction of the gluteal fold, permitting transposition in an unward and medial direction without tension. If muscle flaps are required to help fill very deep defects, they are readily obtained from the adjacent musculature. The authors employed this flap with satisfactory results in 10 cases.

NEUROLOGY & PSYCHIATRY

Review of 75 Intracranial Aneurysms. L. A. Hazouri. J. M. A. Georgia **44:**15-19 (Jan.) 1955 [Atlanta, Ga.].

The cases of 72 patients with 75 intracranial aneurysms were reviewed. Death occurred during the first episode in 46% of 63 cases. Recurrent attacks occurred in 48.6% of this group, that is, the 54% who survived. Five cases of massive subdural hematoma were encountered. Intracranial aneurysm was simulated by two cases of carcinoma, one invasive, the other metastatic. The relative rarity of trauma associated with rupture of an intracranial aneurysm is again noted. Eight cases or 11.1% of aneurysmal rupture with profuse subarachnoid hemorrhage revealed no signs of nuchal rigidity on initial examination. Intracerebral hemorrhage was a prominent postmortem finding in 27 cases, or 42.8%. Gross shift of midline structures that were significant enough to have probably caused a ventriculographic change on x-ray were encountered in 16 cases, or 25.4%.

Bell's Palsy: Report of Three Children Treated with Cortisone. E. T. Wyman. J. Maine M. A. **46:**10-11 (Jan.) 1955 [Portland, Maine].

Disease of the seventh cranial nerve is not infrequent in children; it stems from the same causes that result in facial paralysis in the adult. Bell's palsy may occur in children at almost any age, but it is rare before the age of three. It occurs most frequently between the ages of 6 and 15 years. Three girls, aged 7, 6, and 10 years, respectively, were treated with cortisone in the early stages of facial nerve paralysis. All made complete recoveries two to three weeks after the administration of cortisone was started. While in the past many patients recovered within a few weeks or months, occasionally the paralysis was permanent. No patients in the author's experience have recovered as rapidly as these patients treated with cortisone. The therapy should be started as soon as possible after the onset of the paralysis, before atrophy of the nerve takes place.

Personality Traits and the Normal Electro-Encephalogram. W. McAdam and J. E. Orme. J. Ment. Sc. **100:**913-921 (Oct.) 1954 [London, England].

Correlations have been noted between certain persistent personality traits on the one hand and certain patterns within the normal range of variation of the electroencephalogram on the other. Some of these correlations had been based on impressionistic assessments of personality. McAdam and Orme describe the results of part of an investigation that was under-

taken in order to verify these assessments by a more objective method. Studies were made on 40 male chronic alcoholics who sought treatment. Those in whom there was any suspicion of a concomitant psychosis or of permanent organic disorder were excluded. Some patients were accepted in whom minor signs of organic disorder, such as tremor and slurred speech, were present at the first interview but absent at the second interview and subsequently. If they had not disappeared the case was dropped. The patients were examined 10 days from the day of admission, this period being chosen because preliminary observations seemed to show that a significant degree of intellectual blunting that was present on admission had almost invariably cleared up 10 days later. The personality traits of these men were obtained from a standard psychological interview and from a Ranking Rorschach test and were compared with electroencephalographic tracings. This group did not present any typical personality picture of the alcoholic but rather indicated that, apart from their drinking and its effects, alcoholics have little in common. A dichotomy of personality traits was obtained that appears to be related to the electroencephalographic tracing as a whole and not to any one frequency index. A grouping of qualities suggesting extroversion is apparently related to a predominance of high frequency activity in the electroencephalogram and introversion to a predominance of alpha activity.

Thermal Control in Poliomyelitis. F. M. Allen, F. K. Safford, W. L. Wheeler and others. Arch. Pediat. **71:**354-366 (Nov.) 1954 [New York].

A thermostatically controlled electric unit that circulates fluid at any desired temperature through applicators consisting of two layers of fabric with rubber tubes between them was used for refrigeration treatment of 17 patients between the ages of 4 and 32 years with severe poliomyelitis associated with hyperpyrexia. The patient can lie on such an applicator without disturbance either in bed or in a respirator. A large type of applicator was used for controlling the fever; after restoring the temperature to normal, the large applicator was usually replaced with a narrow "spinal" applicator for reducing the local spinal cord temperature as low as possible. Two of the patients with the bulbospinal paralytic type of disease, with severe weakness of the extremities and dangerously rising temperature, died, but in one of them refrigeration may have temporarily prolonged life. In five patients, two with the bulbospinal paralytic type and three with the spinal paralytic type of disease, there was progression of weakness of muscles. An immediate total arrest of the infection cannot result from refrigeration. Even if it should slow the multiplication or stop the migration of the virus, it can hardly be expected to save nerve cells that already have been invaded. Treatment in these five patients was mostly cautious and intermittent, and it seldom rigidly maintained normal temperatures. Progression of weakness of muscles possibly was limited by thorough treatment in two patients, in one of whom refrigeration was continued for 53 hours, while in the other it was continued with brief intervals for three days. In the three other patients it was not possible to decide whether the influence of refrigeration on progression of weakness of muscles was beneficial, harmful, or indifferent, or whether more thorough treatment might have improved the results. In the remaining 10 patients progression of weakness of muscles was arrested. While it cannot be proved that this was due to refrigeration, the records of these patients at least contributed to the evidence that no serious harm is to be feared. The fever of poliomyelitis is not of the resistant type but can be controlled readily and to any desired degree by the method described. The number of patients treated is too small for evaluating the problem of retardation of the specific infection. Theoretical considerations and the evident harmlessness of the method warrant larger clinical trials. Two benefits of refrigeration are claimed as positive, theoretically and practically: (1) control of hyperpyrexia, which is always harmful and occasionally fatal; (2) relief of the respiratory burden on weakened respiratory muscles, which is the result of the increased metabolism of fever and is particularly serious for patients placed in respirators.

Wilson's Disease—Chronic Form: Clinical-Pathological Observations in a Brother and Sister. B. W. Lichtenstein and I. Gore. A. M. A. Arch. Neurol. & Psychiat. **73:**13-21 (Jan.) 1955 [Chicago].

Lichtenstein and Gore use the term Wilson's disease because they feel that the designation hepatolenticular degeneration is somewhat misleading, because the changes in the brain are not limited to the lenticular nuclei. The chronic form of Wilson's disease is often mistaken for multiple sclerosis or chronic encephalitic paralysis agitans (Parkinsonism) until its true nature is determined by the recognition of the characteristic pigmented ring at the corneoscleral junction and the clinical evidence of cirrhosis of the liver. The chronic type has often been referred to as the pseudosclerotic form, but the authors feel that the designation "chronic" is to be preferred. They present clinical and pathological observations on a brother and sister who had the chronic form of Wilson's disease. They died at the ages of 38 and 37 respectively. The brother's illness was of more than 12 years' duration, and cerebellar symptoms were so prominent that, for many years, he was considered to be suffering from multiple sclerosis. The sister's illness was of at least seven years' duration, its onset being characterized by hemi-Parkinsonism. Both had Kayser-Fleischer rings and multilobular cirrhosis of the liver. Another sister, who exhibited tremor of the upper extremities, died suddenly of massive hematemesis, but four other siblings, as well as the parents, were symptom-free. Studies on the brains of the two patients revealed no gross evidence of cavitation of the lenticular nuclei, but microscopic changes in the form of nerve cell degeneration, shrinkage of the brain tissue with enlargement of the perivascular spaces, and the deposition of lipids, blood pigments, and amorphous debris were present. Pathological alterations were observed in the dentate nuclei, the substantia nigra, and the medulla oblongata. Pericapillary beading and sheathing with calcareous material gave positive stains for copper with Mallory's method. Cerebellar and Parkinsonian signs and symptoms are common in the chronic, or pseudosclerotic, form of Wilson's disease. Remissions occurred in one instance with dimercaprol therapy, but relapses were severe. Hemorrhages may occur in Wilson's disease as the result of esophageal varices or from a hemorrhagic state induced by dysfunction of the liver. The hemorrhagic state may complicate the changes in the brain and lead to a complex pathological picture.

Disturbances in Copper and Amino Acid Metabolisms in Hepato-Cerebral Degeneration and Its Treatment with Dimercaprol (BAL). J. Steger and R. Steger. Deutsche Ztschr. Nervenh. **172:**321-351 (No. 4) 1954 (In German) [Berlin, Germany].

The Stegers point out that the disease originally connected with the names Westphal, Strümpell, and Wilson, and in which hepatic cirrhosis is connected with an extrapyramidal symptomatology, has been designated as hepatolenticular degeneration. Since, however, severe glial changes have been observed in nearly all parts of the brain, including the cerebellum, Schaltenbrand had suggested the more inclusive term "hepatocerebral" degeneration. The essential nature of the disease is still under discussion, and the authors review literature reports that suggest hypoglycemia as a possible causal factor and other investigations that were concerned with disturbances of the mineral, water, and protein exchanges. The discovery by American and British investigators of disturbances in the copper metabolism and of amino-aciduria, and of the fact that these disturbances can be influenced by dimercaprol, induced the Stegers to study the amino acids and copper in the serum and urine during and after treatment with dimercaprol of five patients with established hepatocerebral degeneration, whose histories are presented. The authors found that the metabolic disturbances in hepatocerebral degeneration can be traced to hepatic damage. They ascribe the fact that, by means of electrophoresis and following concentration of urine, they were often able to demonstrate proteinuria to a generalized impairment of the membranes. The observations on the five patients with hepatocerebral degeneration (three with Wilson's disease and two with pseudosclerosis) corroborated that amino-aciduria and increased elimination of copper in the urine are essential characteristics of the disease. The dimercaprol test served as an additional

differential diagnostic criterion in that within four hours after an intramuscular injection of 200 mg. of dimercaprol the urinary elimination of copper increases greatly in patients with hepatocerebral degeneration but not in other patients. The administration of massive doses of dimercaprol effects a considerable elimination of copper. The slight increase in the copper content of the serum probably results from the mobilization of the abnormally stored copper in the tissues. A noticeable clinical improvement, particularly as regards the tremor, was observed even in the patients with advanced lesions. This result is only temporary, a fact that requires intermittent repetition of the treatment. The amino-aciduria is not significantly influenced by dimercaprol.

Hepatolenticular Degeneration: Clinical and Pathological Report of Case Treated with BAL. N. Raskin and J. M. Mackenzie. J. Nerv. & Ment. Dis. **120**:176-183 (Sept.-Oct.) 1954 [New York].

Raskin and Mackenzie present the history of a man, aged 28, who first noticed progressive difficulty in enunciating words at the age of 20, in 1944. A year later there was slurred speech, a slight drooping of the left corner of the mouth, poor coordination, and a coarse intention tremor of the right hand. A Kayser-Fleischer ring was present. In 1946 tremor appeared in both upper limbs and his speech became unintelligible. In 1947 his right limbs and trunk became rigid. In 1949 he had great difficulty in walking and there was bilateral ankle clonus. The resting urinary output of copper was 11 mcg. per hour; this increased to 101 mcg. per hour in the first hour after a single dose of dimercaprol, 2.56 cc. given intramuscularly, representing 4 mg. per kilogram of body weight. In the following two years he received several courses of dimercaprol injections, which produced temporary improvement. The patient died two years after the discontinuation of dimercaprol therapy. The neuropathological findings at autopsy did not differ from those in untreated cases. This suggests that clinical improvement was due to an increased elimination of copper produced by dimercaprol during the treatment period. In the two years following the treatment there was reaccumulation of copper as shown by the chemical analysis of the brain and liver tissues. It seems that continuous maintenance treatment with dimercaprol is indicated.

With Reference to 257 Retrogasserian Neurotomies: Difficulties of the Problem of Essential Neuralgia of the Trigeminus. R. Leriche. Presse méd. **63**:1 (Jan. 1) 1955 (In French) [Paris, France].

A review of the author's experience with retrogasserian neurotomy and that of Pierre Wertheimer as presented in a recent publication shows that there are certain as yet unresolved difficulties connected with the treatment of essential neuralgia of the trigeminus. First, to what should one attribute the comparative frequency of recurrence, even when the root has been completely severed? A priori, one can only suppose that there is some irritation affecting the nuclei of the cerebral trunk, some central excitation, but, if that is so, how can the exposing of Meckel's cavity and the passing of a bistoury over its floor lead to permanent cessation of the crises? How can the fact that extraction of the supra or suborbital nerve or an injection into the foramen of the nerve may be followed by sedation of pain be explained? Some peripheral excitation must be present in these cases, but where is it exerted and where are the bipolar cells that control it? Leriche sees no possible answer to these questions, and this leads him to consider briefly the mechanism of genuine trigeminal neuralgia. The theory that the pain fibers are specific has recently been advanced, but even if their specificity is conceded, the fact remains that the pain-producing stimuli in trigeminal neuralgia—heat, cold, a current of air, rubbing, movement of the lips—are not of a kind to be picked up by nerve endings specialized for the reception of pain. Are there, then, excitants that, though outside the thalamus, can be identified as pain-producing? Quite incomprehensible, too, is the mechanism responsible for the lightning pain caused by fibroma of the Gasserian ganglion, which is relieved by its removal. All of these questions and difficulties should be given attention in any consideration of pain and its mechanisms.

Decerebrate State in Children and Adolescents. R. C. L. Robertson and C. Pollard Jr. J. Neurosurg. **12**:13-17 (Jan.) 1955 [Springfield, Ill.].

Clinical signs of decerebrate rigidity may result from a variety of intracranial lesions in both adults and children. Profound unconsciousness, extensor rigidity in the arms and legs, bilateral Babinski sign, and pinpoint pupils indicate a severe lesion at the midbrain level, whereas the presence of flexion of the arms rather than extension and the tonic neck and labyrinthine reflexes of Magnus and de Kleyn have been said to represent a state of decorticate rigidity. Actually, little distinction between decerebrate and decorticate is made clinically, and in most instances of brain stem and/or midbrain lesions the rigidity is designated decerebrate, although this is not entirely accurate. In clinical practice, most patients are probably in the decorticate state and have associated lesions, such as cerebral laceration, intracranial hematoma, increased intracranial tension, vascular hemorrhage or thrombosis, or a degenerative process secondary to anoxia. Signs of associated injury to the hypothalamus may occur with sham rage, diabetes insipidus, loss of thermal control, reflex chewing, laughing and crying, and marked personality changes, as well as alterations in sleep, blood pressure, pulse, respiration, and sphincter control. Periodic episodes of profuse sweating and excess production of bronchial secretions are signs of dysfunction of the autonomic nervous system. These are observed in nearly all instances of the decerebrate or decorticate state. The present report is a study of the fates of a consecutive group of 13 adults and 13 children. All of them had clinical signs of rigidity, probably most often of high or decorticate type. The authors have been surprised to find that 6 of the 13 children do not have the serious permanent neurological impairment usually considered inevitable when the decerebrate state is definite. These six children recovered to an approximately normal neurological state, a result that was not observed in an adult. All of the children who survived have an intellectual level normal for their age. They are in their usual grade in school. The most favorable results have been obtained in patients about 4 to 15 years of age; in the late teens the outcome may closely parallel that of the adult patient. The authors have no children under their care who are neurological wrecks as a result of their once having been in a decerebrate state. Adult patients in such condition are all too common. Not a single one of the adult patients reviewed here has been able to work; in fact, there are only two who can feed and dress themselves and attend to their toilet. The mortality rate from the immediate insult in the child, especially the very young, would probably be as high or higher than in adults. Tracheostomy is advocated as an early measure to control partial respiratory obstruction caused by secretions and to avoid repeated episodes of hypoxia and cyanosis that may increase permanent neurological deficits.

Aneurysms of the Middle Cerebral Artery: Report of Seven Operative Cases: Review of Literature: Evaluation of Surgical Therapy. D. Petit-Dutaillis and H. W. Pittman. J. Neurosurg. **12**:1-12 (Jan.) 1955 [Springfield, Ill.].

According to Petit-Dutaillis and Pittman aneurysms of the middle cerebral artery constitute approximately 30% of all intracranial arterial aneurysms. The authors present their observations on 12 patients with this type of aneurysm. Nine of these were operated on. Obliteration of the aneurysm by means of silver chips or silk suture was done in seven of the cases. Three of these patients are well, two are improved in comparison with their preoperative state, and two died postoperatively. One postoperative death was the result of an extradural hematoma; the other occurred in a hypertensive woman with an enormous intracerebral hematoma. Autopsy in both instances showed the aneurysm properly clipped and the middle cerebral artery patent distal to the aneurysm. The two patients who are improved but not in perfect health are disturbed principally by mild aphasia caused by intracerebral hematoma. Two of the nine patients with middle cerebral artery aneurysms were subjected only to evacuation of an intracerebral hematoma; they died. One patient declined operation, and two died before surgery. The review of 76 patients with aneurysm of the middle cerebral artery collected from the literature revealed that obliteration of the

aneurysm was the procedure that gave the highest percentage of successful results (83%). Ligation of the carotid artery in the neck involved a mortality of 22%. The authors conclude that the preferred method of treatment is intracranial attack, with obliteration of the aneurysm whenever possible.

Parkinsonism and Trauma. J. M. Nielsen and S. L. Marvin. Bull. Los Angeles Neurol. Soc. **19**:193-196 (Dec.) 1954 [Los Angeles].

Nielsen has gradually become convinced that paralysis agitans (Parkinsonism) is an enzyme disease specifically affecting the crucial cells of the globus pallidus and the substantia nigra. This conviction is based on observations in which: 1. The globus pallidus was destroyed bilaterally with the production of only a caricature of paralysis agitans. 2. Surgical destruction of the ansa lenticularis relieved and did not aggravate the condition. 3. Encephalitis, when it causes the condition, does so in an exaggerated manner distinguishable from the degenerative form. The authors cite the histories of two patients that illustrate that when paralysis agitans does follow trauma, a pure picture of degenerative paralysis agitans does not appear. However, trauma may precipitate the syndrome of loss of automatic associated movement with rigidity, mask-like facies, and even tachylalia. The third patient whose case is presented had been working with copper zinc and cadmium but had not sustained a trauma. Mixed radicular and paralysis agitans symptoms referable to the right arm developed in this man. The authors present this case because it shows that if trauma had occurred the symptoms of paralysis agitans might have been ascribed to trauma.

GYNECOLOGY & OBSTETRICS

Treatment of Pruritus Vulvae and Ani with Injections of Alcohol. W. v. Massenbach and K. Müller. Deutsche med. Wchnschr. **80**:16-17 (Jan. 7) 1955 (In German) [Stuttgart, Germany].

Subcutaneous injections of a total amount of 6 to 8 cc. of 96% sterile alcohol into the itching cutaneous area (0.2 cc. per one square centimeter of skin) were made with the aid of hexobarbital (Evipal) sodium anesthesia in 214 women with pruritus vulvae and ani the causation of which could not be established. Of the 214 patients, 195 were followed up for six months to seven years, while the remaining 19 were lost. Ninety-two of the 195 patients were cured; 67 were improved considerably, 39 of them after one injection, 24 after two injections, 3 after three, and one after 4 injections; treatment thus was effective in 82% of the patients. Thirty-six patients were therapeutic failures although the injections were repeated four to eight times. Careful study of the therapeutic failures revealed diabetes mellitus as the cause of the continued itching in 5, extensive eczematous changes of the vulva and of the perianal tissue in 5, infection with Oxyuris in 6, and a refractory viscid discharge and colpitis in 12, while mental origin was considered in 3. These 31 patients, therefore, did not have essential pruritus vulvae. The cause of the failure could not be determined in five patients only. Complications in the form of small abscesses in the area of the injection occurred in 42 women, but did not involve any risk. Permanent disturbances such as anesthesias did not occur after the treatment in any of the patients. Treatment may be repeated in cases of recurrences after several months. The simple technique makes ambulatory treatment possible. Intracutaneous administration of alcohol must be carefully avoided to prevent necrosis and abscess formation. The subcutaneous injection will be ineffective if the alcohol is injected too deeply into the subcutaneous adipose tissue.

Aspects of Embolism Due to Amniotic Fluid. I. Martin. Frankfurt. Ztschr. Path. **65**:467-477 (No. 4) 1954 (In German) [Munich, Germany].

The case concerned a woman, aged 43, who was hospitalized for delivery on Oct. 21, 1953. She had had three previous normal childbirths, the last 11 years before. Labor pains in the present delivery began 18 days after the estimated date of delivery. At the time of admittance, about six hours after the onset of pains, they were of more than average intensity; the uterine os was dilated to a degree that a finger could be passed, and the amniotic sac was intact. Delivery seemed to advance normally, when suddenly, about three hours after admission, the woman complained of dyspnea and vertigo, became restless, and lost consciousness. When 20 minutes later her condition had not improved, an episiotomy was done and the child delivered by forceps. The severe asphyxia did not respond to treatment and the child died 25 minutes later. The mother died 10 minutes after delivery. The microscopic examination of the fluid obtained from compressing the lung tissues, which was done according to the author's own method, as well as the histological examination of the lungs definitely demonstrated embolism due to amniotic fluid. The juice obtained from the lung showed yellowish admixtures (as fine as dust). Examination of the heart revealed small thrombi and open foramen ovale. The author surveys the 42 cases of amniotic fluid embolism reported in the world literature and comments on the factors that cause these embolisms. She feels that in all fatalities that occur during or after delivery the lungs should be carefully examined for constituents of amniotic fluid; and if the foramen ovale is patent, other vital organs, particularly brain, heart, and kidney should also be studied for evidence of amniotic fluid.

Prolonged Anuria Treated by Infusion into the Vena Cava. J. A. Chalmers and H. T. Fawns. Lancet **1**:79-82 (Jan. 8) 1955 [London, England].

Chalmers and Fawns present the case of a woman, aged 44, who was hospitalized for repair of a uterine prolapse. She was given an intravenous transfusion of one pint of group-O Rh-negative blood before operation. During the operation there was considerable bleeding, and it was decided to continue the transfusion. Blood had previously been cross matched for her, but through an error the blood that was sent to the operating theater was for another patient. This blood was group-A Rh positive, and the mistake was unfortunately not discovered until 300 ml. had been administered. Twelve hours later the patient had secreted only 1 oz. of urine, so the Bull regimen of dextrose and peanut oil by intragastric drip was begun. During the next eight days the urinary output remained very low. Vomiting was troublesome from the second day, and on the eighth day when her blood urea level had reached 361 mg. per 100 ml., she began to have profuse diarrhea. The appearance on this day of the report by Russel and co-workers on the management of prolonged anuria by continuous infusion into the vena cava, prompted the authors to revise their plan. After 10 days of the Bull intragastric drip regimen, infusion into the vena cava was substituted for the next 10 days, and this made possible extensive biochemical control of fluids and electrolytes until diuresis began. The constitution of the infusion was adjusted daily to give an adequate fluid intake, to maintain a reasonable alkali reserve, to insure a sufficient calorie intake, and to achieve a balance of sodium and potassium. To prevent thrombophlebitis, 15,000 units of heparin was added daily to the 40% glucose solution. Heparin was not added to the less concentrated solutions. The infusion into the vena cava enabled prompt rectification of the acidosis with M/6 sodium lactate, as well as rapid correction of dehydration resulting from the diarrhea, which could not have been possible with a peripheral venous infusion.

Carcinoma of the Cervical Stump. J. R. Dodds and J. P. A. Latour. Am. J. Obst. & Gynec. **69**:252-255 (Feb.) 1955 [St. Louis].

Nine hundred ninety-seven cases of carcinoma of the cervix were treated at the department of obstetrics and gynecology of the Royal Victoria Hospital in Montreal, Canada, between 1926 and 1953. Seventy-five were cases of carcinoma in residual cervices, a ratio of 7.5%. Other series of stump carcinoma published to date are relatively small and show some wide variations in their incidence ratio of from 2.6% to 8.1%, as compared with carcinoma of the cervix when the body of the uterus is present. The authors feel that combining the reported series or analysis of larger series will cancel out the spurious deviations and make carcinoma of the cervical stump not significantly different in any way except for the method of treatment. A combined incidence of 7 or 8% of stump carcinoma together with the steady decline in mortality and morbidity associated with total hysterectomy makes this operation mandatory today. The

authors agree with Tice that there is little virtue in separating residual stump cancers from true stump cancers. Both present the same problem in treatment, and this treatment should be by means of radiotherapy when the disease is evident clinically. Carcinoma in situ of the cervical stump can be treated by surgical extirpation. Carcinoma of the cervical stump should be treated by using the same vault dose of radium as in carcinoma of the cervix when the whole uterus is present, and in addition a canal dose should be administered that is proportional to the length of the residual canal. In this way approximately 60 to 70% of the standard dose can be used in stumps. All patients should have in addition the standard dose of external irradiation with few exceptions. Results of adequate treatment of carcinoma of the cervical stump were as good as those obtained in treatment of carcinoma of the cervix when the whole uterus is present. The incidence of vesicovaginal and rectovaginal fistulas as the only definite and readily observable complications of irradiation therapy for purposes of comparison between different series were not significantly higher in the 75 cases of stump carcinoma than in the nonstump cases.

The Lay Use of Potassium Permanganate as an Abortifacient. F. D. Wanamaker. Am. J. Obst. & Gynec. **69**:259-264 (Feb.) 1955 [St. Louis].

Chemical burns on the posterior fornix, the posterior surface of the cervix, and the posterior wall of the vagina resulted from the insertion in the vagina of potassium permanganate tablets by 10 Canadian women in order to produce abortion. Of the 10 patients, 2 died, 3 had abortions, 2 continued to term, 2 were shown not to have been pregnant, and one was lost to follow-up. The tablets used were of 5 grain (0.30 gm.) strength, easily procurable at the drug store without prescription. The fatal outcome in two of the patients resulted from erosion of a blood vessel and severe blood loss; it should have been prevented in both patients. The damage by potassium permanganate will depend on the amount of the chemical used, the concentration, the length of time that it is permitted to act, and the site of injury. When used locally the initial necrotizing effect is usually attended by severe pain, and the patient as a rule seeks medical aid quickly. By the same token the diagnosis can easily be missed, as the patient presents herself with vaginal bleeding, abdominal pain, and a history of having missed one or more menstrual periods. The findings, however, of continuous, severe suprapubic pain, associated with bright red bleeding from the vagina, and particularly if the bleeding is intermittent and associated with shock, should lead to the suspicion of a chemical burn to the vagina. Speculum examination will always establish the diagnosis provided that care is taken to visualize all parts of the vaginal vault. Superficial ulcers may require no treatment, or at the most firm packing for 48 hours. Deep ulcers will require suturing; otherwise, firm packing of the vagina for 48 to 96 hours is indicated. The patients should be observed for a longer period of time than those with uncomplicated abortion because of the danger of secondary hemorrhage from the ulcers. A small amount of distortion and heaping up of the vaginal mucosa can be seen at the site of the ulceration following complete healing. The medical profession should be made conscious of the increasing frequency of this method of attempted abortion. The unrestricted sale of potassium permanganate should be curtailed, as this chemical can no longer be considered a necessary part of the present-day therapeutic armamentarium.

PEDIATRICS

Electroencephalographic Study of Premature Infants. A. Galdó, D. Cabrerizo and M. Cruz. Rev. españ. pediat. **10**:607-618 (Sept.-Oct.) 1954 (In Spanish) [Zaragoza, Spain].

The material of Galdó and collaborators' study consists of 24 electroencephalograms of 14 premature infants, while awake. Most of the infants were born between the seventh and eighth month of pregnancy and a few after the ninth month of pregnancy. The infants weighed between 1,500 and 2,200 gm. at birth. The electroencephalograms were taken in the bipolar leads, with all the necessary precautions for age and prematurity of the infants, when they were between the ages of 1 week and 7 months. It was observed that regardless of the degree of prematurity, cortical electrical activity could be observed. Immaturity of the cerebral cortex is in relation to the weight of the body at birth and to the calculated weight of the brain. From birth to the seventh month of life there is a slow but progressive maturation of the cortex that shows by the increased frequency and parallel diminished voltage of the waves in the electroencephalogram. The rhythm of frequency ranges from 1 to 3 cps during the first few weeks after birth to 7 to 9 cps in the seventh month of life, whereas the voltage lowers during the same period of time from 50 down to 20 μv. The tracings of electroencephalograms of premature infants taken while the infants were awake were very similar to each other during the period of maturation of the cortex. Only the waves of the greatest frequency are regarded. The electroencephalograms manifest that cortical maturity occurs in and progresses from the occipital region. Maturation of the cortex, as shown by the rhythm and regularity of the cortical waves, occurs in the seventh month of life of the infants. This is the first time in which electroencephalograms are taken of premature infants while awake. The electroencephalograms taken on these conditions are of an easy interpretation and of great importance showing the course of cortical maturation.

Resuscitation of the New-Born Infant: A Preliminary Clinical Report on the Use of a Detergent and a Spreading Factor as Aids in Pulmonary Expansion. A. Bloxsom. Anesthesiology **16**:41-47 (Jan.) 1955 [Philadelphia].

It has been suggested that there might be more than just surface tension that counteracts the entrance of air into the lungs of newborn infants and that possibly a cell-cementing substance such as hyaluronic acid found normally between cells of the body may be present as an inhibitor to the expansion of some atelectatic alveoli. These suggestions and the recent favorable reports on the use of the nontoxic detergent, alevaire, in pulmonary therapy induced Bloxsom to use this detergent both as a primary agent and as a vehicle for aerolization of a spreading factor such as hyaluronidase in the treatment of the atelectatic lungs of the handicapped newborn infant. This preliminary report is based on the treatment of a group of infants showing symptoms of atelectasis and hyaline membrane disease by this method. The infant is placed in a nebulized fog of alevaire and an hyaluronidase (alidase), using 500 units (one vial) of alidase to every 500 cc. of alevaire. The nebulized fog is produced in an air lock or incubator by a suitable nebulizer. The infant is left in the fog of alevaire and alidase until all symptoms of respiratory difficulty disappear. The author feels that the clinical results from the use of a combination of a detergent and a spreading factor in the treatment of atelectasis and clinical hyaline membrane disease in the five reported cases warrant a further trial of this method of therapy as an aid to pulmonary expansion in the resuscitation of the newborn infant.

Management of Hemophilus Influenzae, Type B, Meningitis: Analysis of 128 Cases. R. Koch and M. J. Carson. J. Pediat. **46**:18-29 (Jan.) 1955 [St. Louis].

Seven hundred fifty-eight patients with meningitis have been treated at the Los Angeles Childrens Hospital from 1930 to 1953. A detailed analysis revealed: a tuberculous origin in 168 cases, Hemophilus influenzae in 128, meningococcus in 126, pneumococcus in 98, and miscellaneous causes in 238 cases. The authors present an analysis of the 128 patients with meningitis due to Hemophilus influenzae, type B. The ages of the children ranged from 7 weeks to 12 years. Fifty patients were less than one year old. Sixty per cent of the patients were males. Bacteriological studies disclosed H. influenzae in 28 of 56 nasopharyngeal cultures and in 53 of 74 blood cultures. Spinal fluid cultures were positive in 116 of 128 cases, and in the other 12 patients the diagnosis was based on positive blood or nasopharyngeal cultures. Spinal fluid cell counts ranged from 2 to 20,000 per cubic millimeter. Differential cell counts usually revealed 80 to 100% polymorphonuclear forms. The first 14 patients, receiving only supportive measures, all died within two weeks of admission to the hospital. They all had septic temperatures, vomited frequently, fed poorly, became progressively more spastic and lethargic, and had frequent convulsions.

Daily spinal drainage afforded relief until block occurred, usually followed by death within 40 to 72 hours. Terminal pneumonia and mastoiditis were frequent findings at autopsy. There were 2 survivors among the 13 patients who were treated with sulfonamide alone. The combination of sulfonamide plus Alexander's rabbit antiserum was employed in 12 patients, with 2 deaths. Residuals of mental retardation, blindness, hydrocephalus, and convulsions occurred in 20% of the survivors. Hospitalization averaged four to five weeks. In 1946, streptomycin was introduced, and in 27 patients the combination of sulfonamide, streptomycin, and rabbit antiserum was used. There were two deaths; residuals in the form of hydrocephalus, convulsive disorders, mental retardation, or deafness occurred in 6 of the 27 patients, and recurrences were noted in two patients. The average length of hospitalization was three weeks. Oxytetracycline was first used in 1949, and 46 patients received it in combination with streptomycin and sulfonamide. There were two deaths, and residual complications were also observed in two patients. Hospitalization averaged two to three weeks, and there were no relapses. Chloramphenicol has not been routinely used, but the last group of 16 patients with no deaths received this drug in various combinations with others. This is a particularly difficult group to evaluate as no over-all single plan was utilized. The histories of five of these patients are presented, and the authors feel that chloramphenicol has added nothing to their standard treatment, which employs a combination of sulfonamides, streptomycin, and oxytetracycline. Subdural effusions were known to be present in eight patients during life. Six cleared with repeated taps, one with surgical irrigation, and one required removal of membrane. An additional subdural effusion was found at autopsy. Subdural taps should probably only be done for specific cause and not routinely.

Tetanus Neonatorum. G. van Haesebrouck. Maandschr. kindergeneesk. **22**:415-417 (Dec.) 1954 (In Dutch) [Leiden, Netherlands].

The infant boy whose case is presented had been delivered by a normal birth, but the umbilical cord had been tied by an untrained person. On the fourth day the infant refused to nurse, and convulsive symptoms appeared. In the afternoon of the same day the family physician was called, who at once diagnosed tetanus and hospitalized the infant. Meningitis and cerebral hemorrhage were excluded by spinal puncture. The umbilicus was necrotic and gave evidence of severe infection. The infant was put in a quiet, darkened room, 50,000 units of antitetanus serum was injected intramuscularly, and 100,000 units of penicillin was injected intramuscularly every three hours. Chlorpromazine (Largactil) was given on the first day three times in 5 mg. doses, and beginning with the second day five times daily in 5 mg. doses. In addition 60 mg. of phenobarbital (Luminal) was given. The child was fed with mother's milk by nasal tube. On the second day an additional dose of 20,000 units of antitetanus serum was given. Trismus was lessened four or five days after onset of treatment; opisthotonus persisted for only a few days, and the general stiffness subsided after about 10 days. Feeding by tube could be stopped after 22 days. The chlorpromazine doses (five times daily 5 mg.) were gradually reduced after the 10th day, but the 60 mg. daily dose of phenobarbital was continued for 25 days, at which time practically all signs of tetanus had subsided. At the time the infant was discharged he had not only regained the weight lost during the first period of tube feeding but had gained 600 gm. The author feels that treatment with chlorpromazine contributed to the favorable outcome.

Severe Nursery Epidemic Associated with Esch. Coli Type 111 B4. W. B. McClure. Canad. M. A. J. **72**:83-85 (Jan. 15) 1955 [Toronto, Canada].

Several epidemics of gastroenteritis have occurred in nurseries in Ontario, Canada, in the past few years. Most of these were caused by some strain of colibacillus, e. g., Bacterium coli neapolitanum, which was described in 1945 by Bray. A report is made of one of these Ontarian epidemics; this one occurred in one hospital of a medium-sized town in 1953. From Jan. 1 to Dec. 12, 1953, 51 infants under 2 months of age were admitted to the hospital for gastroenteritis; 45 of them had been born in the hospital, and 15 died. A visit to the hospital by medical representatives of the Ontario Department of Health revealed that the methods of isolation used with respect to the infants left much to be desired and that the infection could have been transmitted by means of feeding bottles, since these were taken back to the formula room after use without first being sterilized or washed. Breast feeding was not encouraged in the hospital and was not widely practiced. The administration of antibiotics and of solutions interstitially or intravenously to combat dehydration was inadequate and failed to prevent the high mortality among the infants. Treatment was not standardized but was left up to the individual physician. In the majority of cases, Escherichia coli, type 111 B4, was recovered from the stools. The organisms displayed in vitro resistance to streptomycin and the sulfonamides but were sensitive to chloramphenicol and, to a lesser degree, oxytetracycline. The epidemic was finally put under control through the use of strict isolation techniques, immediate sterilization of feeding bottles after use, substitution of liquid hexachlorophene soap for cake soap in staff washrooms, and adequate, even preventive, antibiotic therapy based on frequently obtained stool cultures.

Ossifying Fibromas (Fibrous Dysplasia) of the Facial Bones in Children and Adolescents. N. Georglade, F. Masters, C. Horton and K. Pickrell. J. Pediat. **46**:36-43 (Jan.) 1955 [St. Louis].

Georglade and associates review observations on 34 patients with fibrous dysplasia who were treated at Duke Hospital, Durham, N. C., during the decade from 1944 to 1954. Twenty of these patients were under 18 years of age. The maxilla was involved in approximately 70% of the patients. The mandible was found to be involved in 20% and the ethmoidal and orbital regions in the remaining 10%. The youngest child was 4 years of age. Twenty-four of the patients were females. The origin of ossifying fibromas is still in doubt, but there are two main groups of thought. One group suggests that these tumors arise only from membranous bone, as found in the face and skull. The second group believes that an ossifying fibroma is a variant of monostotic fibrous dysplasia. These benign growths may cause considerable deformity, even proptosis and general displacement of the orbital contents. There may also be marked enlargement of one side of the face, with or without impairment of vision. In the mandible the growth process may be extensive and resemble an adamantinoma. Painless swelling was the most uniform complaint. The microscopic appearance of these growths varies greatly. Some classify them into different histological types depending on the degree of maturity, the least differentiated type being rich in cellular connective tissue with many osteoid clumps, centrally calcified, and peripherally poor in calcium. The other groups become progressively acellular with a greater proportion of functionless bone in each succeeding category, and the most mature type is classified as an osteoma. The degree of calcification and the amount of osteoid substance will influence the radiopacity. A careful radiological technique is necessary to avoid mistaking ossifying fibroma for a dentigerous cyst, fibromyoma, giant cell tumor, or adamantinoma. In the cases reviewed, the patients with maxillary involvement revealed considerably more radiopacity by roentgenogram than did patients with mandibular involvement. Some of the mandibular tumors had areas of decreased density with cyst-like characteristics. The surgeon is confronted with the alternative of either removing the tumor as completely as possible through an external approach or using an oral approach, which affords less visibility to the tumor mass. The authors observed a tendency to recurrence when they used the most conservative surgical treatment. In three of their patients reshaving of the involved bone through an oral approach became necessary every few years. Conservatism is the method of choice with slow growth. When there is maxillary involvement and the process can be recontoured through an oral approach, a modified Caldwell-Luc approach is utilized. If an oral approach is not feasible because of the size or location of the growth process, a modified Fergusson approach is easily performed, yielding an adequate exposure with minimal scarring postoperatively.

The Management of Acute Leukemia in Childhood. J. H. Burchenal and M. L. Murphy. New York J. Med. **54:**3362-3365 (Dec. 15) 1954 [New York].

Three types of therapeutic agents are available for the treatment of acute leukemia in children: (1) the folic acid antagonists of which methotrexate (amethopterin) and aminopterin are examples, (2) the purine antagonists of which mercaptopurine and thioguanine are examples, and (3) the adrenal cortical hormones of which cortisone and corticotropin are examples. In deciding which of these types of drugs to use in a given case of acute leukemia, the following facts should be taken into consideration: 1. The antimetabolites cause longer and more satisfactory remissions but take three to eight weeks to exert their beneficial effects. 2. The steroid hormones act much more rapidly than the antimetabolites, but the remissions produced are of relatively short duration. 3. There is no cross resistance between the three different classes of agents, and patients whose disease has become resistant to one may still respond to others. Thus, the steroids must be used in patients who are acutely ill and need rapidly acting therapy, while the antimetabolites may be reserved for less desperate cases. Eventually in the course of a child's disease, all three types of medicaments can be used to induce various remissions. Evidence that these agents have lengthened survival time is provided by the following statistics: In 218 untreated cases of acute leukemia in children collected from the literature by Tivey, 50% of the patients survived 3.9 months from the start of their disease and only 5% were alive 12 months after the onset. Of 154 children with the same disease treated at the New York Memorial Hospital with the folic acid antagonists and/or the steroids before the advent of mercaptopurine, 50% survived 8.9 months from the start of their disease and 29% were alive at 12 months. Of 52 children treated by the authors in the manner described since mercaptopurine became available, 50% survived 12.5 months and 52% were alive at 12 months after the start of their disease.

DERMATOLOGY

Turban Tumor. C. D. Evans. Brit. J. Dermat. **66:**434-443 (Dec.) 1954 [London, England].

Two cases of turban tumor are described. Both occurred in women, aged 58 and 43 respectively. Turban tumors are cylindromas that occur on the head in such numbers as to cover the scalp more or less completely. Individual tumors vary in size from a few millimeters to 4 or 5 cm. in diameter and may be grouped in bunches. The tumors grow slowly and are benign. The patient, who was 58 years of age at the time of treatment, reported that at the age of 16 she had had a small lump on the neck. This did not increase in size until later, when other lumps appeared. When she was 38 she noticed a small lump on the scalp, and shortly afterwards another appeared in the region of the umbilicus. About three years later that on the scalp had grown to the size of a walnut and the other was the size of a tangerine orange. These were excised. By the age of 44 many other small lesions, the size of a pin's head, were present on the scalp, forehead, temples, ears, and nose. Within a few months others appeared on the upper abdomen, back, and genital area. She said that the tumors grew much more rapidly after the menopause. The second patient had first noticed small tumors over the hairy scalp at the age of 23. Both patients were treated by removal of the tumor-bearing areas of the scalp followed by Thiersch grafting. The large tumors scattered over the body in one case were excised. The histological pictures of Brooke's disease and turban tumor are identical except for the membrane surrounding the clumps of tumor cells in the latter disease. This membrane is probably composed of a glycoprotein or glycolipin secreted by the tumor cells. X-ray treatment, with doses just sufficient to cure basal cell carcinoma, severely disorganized the tumors but did not cure them. Five months after treatment the tumors were beginning to recover their normal histological appearance. Experiments to ascertain the presence of cutaneous carcinogens in the tumors was carried out with extracts of the tumors painted on to mice. No malignant tumors occurred, but premalignant changes were seen. Turban tumors may be nevoid in origin and arise in cell rests from the stratum germinativum that would normally form apocrine glands.

Keratoderma Punctatum Syphiliticum: Report of a Case. F. Kerdel-Vegas, A. W. Kopf and J. A. Tolmach. Brit. J. Dermat. **66:**449-454 (Dec.) 1954 [London, England].

Kerdel-Vegas and associates present the case of a man, aged 33, who when seen in April, 1954, reported that during the previous six months there had developed on his palms and soles, and on the volar aspects of his fingers and toes, asymptomatic, firm "warts" presenting central plugs and pits. Some of these plugs were either spontaneously extruded or picked out of their sockets by the patient, thereby leaving deep, punched-out 1 to 2 mm. pits with smooth bases. The patient said that he had had many more such lesions on his palms, and that they disappeared spontaneously during the first month of his ailment. He further stated that at the time of the first eruption on his palms and soles in November, 1953, he had laryngitis with severe hoarseness. At that time he also noted tender subungual lesions, which became asymptomatic in one week. Following a period of quiescence, he noticed a patchy alopecia, and recurrence of the hoarseness in March, 1954, five months after the onset of his illness. At examination it was found that the lesions were symmetrically distributed and showed no tendency to coalesce. Point pressure on the papules caused no discomfort. Several of the finger and toenails showed discrete subungual hyperkeratoses and transverse ridging of the nail plates. The results of the serologic tests for syphilis and the immune-adherence test of Nelson were strongly positive. Histological changes consisted essentially of a parakeratotic plug, thickening of the dermal vessels, and a perivascular plasma-cell infiltrate. The patient was treated with 9 million units of penicillin over a period of 15 days. Ten days after the onset of treatment, the papules became softer and flatter and the pits more shallow. Gradually the lesions disappeared. The authors point out that in addition to syphilis, other dermatoses can produce the identical clinical picture of keratoderma punctatum including: Lichen planus, Darier's disease (keratosis follicularis), porokeratosis of Mibelli, keratoma periporale of Gans, verruca vulgaris, arsenical keratoses, and drug eruptions (e. g., streptomycin). This case fits the description of keratoderma punctatum, and morphologically it cannot be differentiated from the nevoid variety. At the time the patient was seen no other clinical manifestations of secondary syphilis were found, and the true diagnosis was established only after serologic and histological examinations. In regard to the latter, the epidermal changes are identical with those seen in the idiopathic forms of keratoderma punctatum, but the perivascular plasma-cell infiltrate and thickening of vessels are not seen in the nonsyphilitic punctate keratodermas.

Pyoderma Gangrenosum in Association with Chronic Ulcerative Colitis. H. A. Brunsting. Ohio M. J. **50:**1150-1151 (Dec.) 1954 [Columbus, Ohio].

Brunsting reviews the present status of knowledge on pyoderma gangrenosum, which he defines as a fulminating ulcerative disease of the skin, which appears in patients with chronic ulcerative colitis. While the occurrence of infectious gangrene of the skin in association with debilitating systemic disease, especially dysentery, has been recorded in the literature during the past century, Brunsting, together with Goeckerman and O'Leary, was the first to give a detailed description of this syndrome in 1930. They suggested the term pyoderma gangrenosum in a report of five patients, four of whom had chronic ulcerative colitis and one chronic empyema. The incidence of skin manifestations in association with chronic ulcerative colitis has been variously estimated at from 2.4 to 10.7%. The skin disorder usually involves the extremities and the body. The cutaneous pattern may be that of furunculoid lesions, erythema multiforme, exanthematous eruptions, erythema nodosum, or extensive fulminating ulcerative pyoderma. Involvement of the skin may precede the development or recognition of the underlying systemic disorder. There is a parallelism between the skin lesions and the underlying debilitating process. These patients apparently are in a hypersensitive state; the simple trauma of a hypodermic injection may result in cutaneous lesions. At first there may be crops of small, discrete pustules surrounded by an inflammatory areola. The center of the pustule may soften, the overlying skin turning blue and then breaking down. The lesion either undergoes spontaneous involution or extends peripherally

to coalesce with adjoining ones. Healing occurs from the outer zone and results in thin atrophic scars and brownish pigmentation. Discussing the differential diagnosis, the author says that the appearance of crops of pustules, with a circumscribed inflammatory areola, may suggest the diagnosis of ioderma or bromoderma. Blastomycosis, sporotrichosis, coccidioidal granuloma, and other mycotic infections can be ruled out by the absence of typical organisms in smear or culture. The diagnosis of tuberculosis verrucosa cutis, tertiary syphilis, and cutaneous ulcers in association with sickle cell anemia also can be eliminated by lack of confirmatory evidence. The treatment must be individualized. Factors that precipitate periodic relapses must be avoided; these include: fatigue, intercurrent infection, emotional disturbances, and dietary indiscretions. A bland, low-residue, nonlaxative, high caloric diet with adequate protein intake and vitamin supplement is essential. When hypochromic anemia is present, blood transfusions are indicated. The judicious use of the corticosteroids may be of value in selected patients with an associated polyarthritis. The antibiotics exert little effect. Treatment of the underlying debilitating systemic disease is of primary importance in the treatment of pyoderma gangrenosum.

Accidental Wart Auto-Inoculation: Report of an Unusual Case. A. B. Kern. Rhode Island M. J. **37**:680-681 (Dec.) 1954 [Providence, R. I.].

Kern presents the case of a woman, aged 38, who noted a painful lesion on her toe. One month later, while paring this down, she accidentally cut her right index finger with the contaminated razor blade. The wound healed uneventfully within 10 days. About three weeks after the injury, the woman observed the onset of thickening in the scar. This gradually increased in size, becoming raised and painful. Application of Whitfield's ointment had no effect other than to induce redness and scaling of the surrounding skin. The patient was first seen by the author five months after the injury to the finger. On the lateral aspect of the right second toe was a round, yellowish verrucous lesion with several black dots in the center that was elevated and slightly tender. On the ulnar side of the distal phalanx of the right index finger was a linear, slightly curved, yellowish mass that was elevated and moderately tender, with surrounding mild erythema and scaling. At one end were several characteristic black dots. According to the patient, the neoplasm corresponded exactly in its location to that of the original wound. Both lesions were typical warts. This case demonstrates the infectious nature of such lesions.

UROLOGY

Hypercalcuria and Metabolic Bone Disease. M. L. Rosenberg. California Med. **81**:382-390 (Dec.) 1954 [San Francisco].

According to Rosenberg, nephrocalcinosis and nephrolithiasis are the identical urologic end-results of hypercalcuria and all types of metabolic bone disease. The differential diagnosis and proper identification of the primary lesion in most cases of hypercalcuria and renal calcium precipitation will be made with the aid of history, physical examination, a few simple laboratory tests, and roentgen studies of the bones. The first step is to recognize that hypercalcuria is present by measuring the calcium excretion while the patient is on a regulated low calcium intake. There are essentially four causes of hypercalcuria. 1. Increased gastrointestinal absorption of calcium leads to hypercalcuria as a direct result of the excess intake. The blood levels of calcium, phosphorus, and alkaline phosphatase are generally normal, and decreased calcium intake results in rapid improvement. 2. Hypercalcuria caused by excess bone resorption occurs in a group of diseases including hyperparathyroidism, acidosis, osteolytic metastases, multiple myeloma, Paget's disease, and sarcoidosis. Specific treatment, if instituted early, will result in a satisfactory response and prevent the progression of renal complications. 3. Hypercalcuria caused by decreased bone formation occurs with either osteoporosis or osteomalacia. In osteoporosis, there is a defect in tissue metabolism, so that the bones cannot accept the available calcium. The defect may be in the osteoblasts or the bone matrix or on an idiopathic basis. In osteoporosis associated with enforced recumbency or in the most common form of postmenopausal osteoporosis, the serum calcium and phosphorus levels may be high and the alkaline phosphatase level is normal. The skull and lamina dura are normal. Treatment by the Shorr regimen with dietary restriction of phosphorus and administration of adequate amounts of aluminum carbonate or hydroxide, mobilization, and weight-bearing will prevent renal complications. In postmenopausal osteoporosis, combined estrogen-androgen therapy causes dramatic response. Defects in the bone matrix may occur in any state of protein deficiency (malnutrition), scurvy, and conditions in which there is excess antianabolic hormone (adrenal cortical hyperfunction, "alarm reaction," corticotropin and cortisone therapy). Treatment is directed at the underlying condition, and in addition the patient is placed on a high protein diet and testosterone is administered. Senile osteoporosis responds rapidly to steroid therapy. Idiopathic osteoporosis is uncommon and does not respond to steroids. Osteomalacia is a defect involving calcium so that the calcium is not available to the bones. In this condition the serum alkaline phosphatase is high and the serum calcium and phosphorus levels may be normal or low. It may occur from a rare lack of vitamin D, because of an idiopathic loss of calcium in the urine, or secondary to renal acidosis. 4. Excess renal excretion of calcium is largely responsible for renal acidosis of the tubular insufficiency type. It is characterized by hyperchloremic acidosis, with alkaline urine, decreased urinary ammonia, and decreased titratable acidity. Treatment consists of a high alkali intake and administration of calcium and vitamin D in large doses; the response to the treatment is dramatic. Renal acidosis of the Fanconi type also is caused by excess calcium loss in the urine, and the treatment is the same.

The Artificial Kidney and Related Procedures: A Report on Clinical Experience. P. F. Salisbury. California Med. **81**:391-395 (Dec.) 1954 [San Francisco].

The Skeggs-Leonards artificial kidney and related effective dialyzer-ultrafilters were used by Salisbury for 30 dialyses in patients with various types of renal disease. Clinical improvement of varying degree was obtained by this method of treatment that appeared to be lifesaving in four of five patients between the ages of 15 and 56 years with acute renal failure. Treatment with the artificial kidney is indicated for patients with acute renal failure in whom clinical signs of uremia develop. The artificial kidney should be applied before the patient's condition has become irreversible. Removal of edema fluid is possible with modern artificial kidney equipment and appears to extend the therapeutic possibilities of the procedure. There is good experimental and some clinical evidence that the artificial kidney may be lifesaving in intractable cases of barbiturate poisoning, bromide poisoning, and other intoxications caused by diffusible substances. It affords temporary palliation in certain patients with chronic uremia, and it may be used to overcome acute exacerbations of chronic renal disease. The artificial kidney has been used by other workers to advantage to prepare uremic patients for surgical intervention who otherwise could not withstand operation. Artificial kidney procedures should be used with great caution in patients with signs of a bleeding tendency. Although some hemorrhagic conditions such as a bleeding peptic ulcer are not an absolute contraindication, other methods such as replacement transfusion may be used for the radical treatment of patients with acute renal failure and a bleeding tendency.

Needle Biopsy in Diagnosis of Prostatic Cancer. J. J. Kaufman, M. Rosenthal and W. E. Goodwin. California Med. **81**:308-313 (Nov.) 1954 [San Francisco].

One hundred ten patients with clinical indications of cancer of the prostate were subjected to needle biopsy and open perineal or transurethral biopsy. Seventy of the same patients had prostatic smear examination. With the open perineal biopsy or the positive transurethral as the standard, the accuracy of prostatic palpation, prostatic smear, and needle biopsy was determined. A high degree of correlation (74%) was demonstrated between digital rectal evaluation and positive surgical biopsies in both early and late cases. There were 17 false positive clinical diagnoses. The prostatic smear showed an over-all correla-

tion of 45% when compared with the results of positive surgical biopsy. The over-all accuracy of needle biopsy was 73%. However, in the last 39 cases, including 8 in which the carcinomas were in the curable stages, the needle accuracy was 100%. When there is clinical indication of malignant disease of the prostate, needle biopsy of the lesion is warranted and should be done before definitive or palliative treatment is undertaken. The procedure does not require hospitalization and may be done under local anesthesia.

The Ill-Effects of Radiotherapy. D. M. Wallace. Brit. J. Urol. **26**:364-368 (Dec.) 1954 [Edinburgh, Scotland].

The present is one of a series of discussions on irradiation therapy in urology. Wallace feels that the invidious task of discussing the ill-effects of any therapy is a necessary one, if one is to present a fair picture to the protagonists of radiotherapy and surgery alike. He confines his remarks to certain clinical observations that his group made in the treatment of 596 cases during the last four years. The cases are divided into three groups: (1) those treated by external irradiation with high or supervoltage; (2) those treated by interstitial irradiation using radon, radium, radioactive tantalum, or gold; and (3) those treated by means of intracavitary irradiation using radioactive sodium or bromine solution, and by intracavitary irradiation with cobalt. External irradiation may produce harmful effects on the skin, subcutaneous fat, the rectum, or the bladder. The effect on the bladder must be considered before deciding whether it is justifiable to treat a patient palliatively. During the last few weeks of treatment, or during the first month after the completion of treatment, there is a reactionary swelling of the trigone and often obstruction to the ureters. In the presence of a sloughing growth this partial obstruction, with consequent stasis of the urine, appears to predispose to pyelonephritis, which may cause sudden death. The late effects of external irradiation are mainly those associated with the replacement of muscular tissue by fibrosis. Changes in the arterioles and the submucous capillaries are another complication caused by external irradiation. The ill-effect of interstitial implants is predominantly failure to control the tumor, resulting in local recurrence. After intracavitary irradiation the mucosa becomes atrophied, the submucosa becomes congested, and the arterioles become altered, either by a complete endarteritis or by a fibrotic replacement of the arteriolar wall. With this combination it is fairly common to see 6 to 12 months after treatment multiple submucosal telangiectases, which occasionally bleed fairly readily when the bladder is stretched. It has been necessary to remove bladders because of hemorrhage due to this cause. The author concludes that radiation is an extremely destructive weapon in the hands of the inexperienced. With excessive dosage, tumor and normal tissue alike will be destroyed. In the optimal dosage one has a chance of controlling the tumor, but if given in an inadequate dosage, or a dosage that is incorrectly distributed, not merely will the tumor fail to be controlled but subsequent surgery may be rendered more difficult. No amount of irradiation would appear to exercise any influence on the late development of new tumors. It is probably better to avoid interstitial and intracavitary irradiation in small, low grade lesions so long as any conservative method of treatment can be relied upon to give a satisfactory result, because once intracavitary, interstitial, or external irradiation has been used, it is fair to say that no form of conservative surgery can be regarded as safe, and a patient that has failed to respond to radiotherapy must come to total cystectomy.

Spontaneous Regression of Pulmonary Metastases Arising from a Testicular Tumor. M. Malament and W. W. Johnston. J. Urol. **73**:117-123 (Jan.) 1955 [Baltimore].

A case of spontaneous regression of pulmonary metastases, temporary in nature, arising from a teratocarcinoma of the testis with a coexisting chorioepithelioma in a 28-year-old man is reported. For eight months preceding the patient's admission to the hospital he had noticed a progressive painless enlargement of the left testis. Chest roentgenograms revealed multiple metastatic nodules, ranging from 0.5 to 1 cm. in diameter, scattered through both lung fields. A left orchiectomy was performed. The pathological findings revealsd a teratocarcinoma of the testis with few chorioepitheliomatous elements. In view of the abnormal pulmonary findings, irradiation therapy was considered inadequate and not advised. Chest roentgenograms taken three months later revealed no evidence of any metastases. Repeated roentgenograms again showed normal pulmonary findings. None of the previously described metastatic nodules were visualized. Radiation therapy to the regional lymph nodes was advised at this time, but the patient refused further treatment and left the hospital against medical advice. Seven months later, the patient was readmitted to the hospital complaining of pronounced weight loss, anorexia, weakness, and dyspnea on exertion. A chest roentgenogram revealed numerous round, well-defined metastases throughout both lung fields. Roentgen therapy to the recurring metastatic nodules was instituted but was of no avail. The patient deteriorated rapidly and died three months after his readmission to the hospital. The chest roentgenograms of this patient illustrated the changing picture of the pulmonary metastases, their initial appearance, disappearance, and overwhelming recurrence. Roentgen therapy was not a cause of the remission, as it was not utilized. The recurrent shower of metastases, probably from slowly growing retroperitoneal lymphatic metastases, occurred as part of the terminal phase. The literature revealed four different theories regarding the possible etiology of spontaneous remission; whether the antibody, hormonal, self-destructive, or maturation process, or a combination of these can produce these regressive changes has not been determined. Similar cases have probably been seen but not reported.

Sudden Death from Ingress of Barium Sulfate Into Blood Following Urethral Perforation. I. G. Fazekas. Ztschr. Urol. **47**:673-679 (No. 11) 1954 (In German) [Leipzig, Germany].

According to Fazekas, 10 to 20% suspensions of barium sulfate are sometimes used as contrast medium to ascertain site and degree of urethral constrictions. He reports on two men, aged 59 and 70, respectively, in whom a 10% suspension of barium sulfate was introduced for this purpose. A few minutes later they experienced nausea, and signs of shock were evident. Death followed within from 8 to 10 minutes. At autopsy the greatly contracted urethra in one of the patients showed five, and in the other four, perforations, through which barium had entered the corpus cavernosum. Roentgenograms that had been taken immediately after the injection showed characteristic barium shadows in the corpus cavernosum, pudendal plexus, and the vena hypogastrica. Pulmonary roentgenograms made at autopsy showed no shadow indicative of a barium embolism. The presence of barium sulfate in the internal organs was demonstrated by chemical examination. The clinical signs and the results of autopsy and of histological studies indicate that in both men the sudden death was caused by shock, which in turn had been produced by the introduction of barium sulfate into the blood stream through the perforations. The histamine freed by the detached and decaying endothelial cells probably elicited the shock mechanism, resulting in death. Spasms of the pulmonary arteries and of the bronchi were histologically demonstrable in both cases. The introduction of barium into the urethra should be preceded by the introduction of urethral sounds and catheters in order to avoid future fatalities from this cause.

OPHTHALMOLOGY

Treatment of Herpes Zoster Ophthalmicus with Cortisone or Corticotropin. H. G. Scheie and M. C. Alper. A. M. A. Arch. Ophth. **53**:38-44 (Jan.) 1955 [Chicago].

Scheie and Alper report observations on the therapeutic effect of the systemic administration of cortisone and corticotropin in 11 patients with herpes zoster ophthalmicus, all of whom had ocular involvement. The patients had the characteristic, rather severe pain of herpes zoster. All showed the classic signs of iridocyclitis, occurring alone or accompanied by keratitis. Some had secondary glaucoma. In all but one instance, relief of pain was dramatic, nearly always occurring within 24 to 36 hours. Inflammatory ocular signs showed rapid improvement, although in several instances a protracted mild, but recurrent, course

ensued. The symptoms of this protracted rather mild iritis or keratoiritis were usually readily controlled by atropine and cortisone administered locally. Elevated ocular tension likewise usually subsided promptly. In one instance operative intervention was necessary. None of the patients sustained visual loss. It is suggested that the hormones in some way block the response of tissues to the viral agent. In this way they suppress the ocular reaction and prevent serious complications. It is unlikely that cortisone or corticotropin have any specific action against the virus of herpes zoster.

Lipoliquid in Treatment of Hemorrhagic Diabetic Retinopathy. M. R. Folk. A. M. A. Arch. Ophth. **53**:93 (Jan.) 1955 [Chicago].

Recently the liver has been implicated as possibly playing a role in the vascular complications of diabetes mellitus. The fatty infiltration of the liver observed in diabetes is believed to predispose to increased vascular disease. By reducing fatty infiltration by lipotropic substances, and thereby improving liver function, it is hoped that the vascular disease will be arrested. The lipoliquid used in this study contains choline, the most effective lipotropic agent known; inositol; and vitamin B_{12}, believed to be catalysts in the formation of the mobile choline-based phospholipids. Fifty patients with diabetic retinopathy were treated with Lipoliquid. When associated with retinitis proliferans, treatment was completely unsuccessful. About half of the patients without proliferation showed no progression, and the remainder only slight progression. However, this group of patients frequently maintained their visual acuity for a long period of time, and the development of retinitis proliferans in two cases and of recurrent hemorrhages in all cases suggests that Lipoliquid is of very limited value in the treatment of hemorrhagic diabetic retinopathy.

Plastic Lens Insertion After Cataract Extraction: A Series of Cases and Modification of Technique. J. P. Harshman and M. Shusterman. Canad. M. A. J. **72**:15-17 (Jan. 1) 1955 [Toronto, Canada].

Harshman and Shusterman began to perform insertions of plastic lenses in July, 1952, that is, shortly after they learned of Ridley's method, which was described in the *Lancet* (**1**:118 [Jan. 19] 1952; abstracted in THE JOURNAL, May 10, 1952, p. 202). They report the results on 13 consecutively treated eyes (12 patients). The patients ranged in age from 36 to 95 years, but all except three were over 60. Their patients were selected, so that each had to be in reasonably good health, free of diabetes mellitus, and with a mature cataract in an eye with no known intraocular disease. Extracapsular extraction was performed on all patients, using Ridley's technique of plastic lens insertion with their own method of cataract extraction. As regards preoperative mydriasis, the authors found that if the pupil was larger than 5 mm. at the onset, after insertion of the lens they experienced difficulty in positioning the large pupil. Thereafter they used no preoperative mydriatic. A small pupil precluded neither successful cataract extraction nor insertion of the lens. Since their new method of plastic lens insertion has only been performed on the last two patients, it cannot be fully assessed as yet. It has the advantage of causing less iris trauma and therefore less pigment disturbance and exudate. However, there may be some trauma to the corneal endothelium. Insertion of the lens was successful in 12 of 13 eyes. In one patient, the lens became dislocated postoperatively, probably because of the preoperative mydriasis. The removal of this anteriorly dislocated lens offered no difficulty and left the eye in the usual aphakic state. Vitreous loss was not experienced in any patient. As expected with the avascular corneal incision, no postoperative hyphema occurred. Two patients have no peripheral iris openings. Up to the present, glaucoma has not occurred in any patient. Strenuous physical activity in at least one patient has produced no apparent change in the position of the lens over a period of 14 months. The visual results indicate that the operation is successful in patients with mature senile cataracts.

THERAPEUTICS

Cortisone and Antibiotics in Treatment of Extremely Acute and Moderate Meningococcic Infection: Clinical and Prognostic Significance of Circulating Eosinophils. G. Bartolozzi and S. Borgheresi. Riv. clin. pediat. **54**:358-379 (Nov.) 1954 (In Italian) [Florence, Italy].

The action of cortisone and the behavior of the eosinophils were studied in eight patients with meningococcic infection. Initial values of 55 and 66 eosinophils per cubic millimeter were found in the two patients who had typical symptoms of fulminant meningococcic infection. These initial eosinophil values were considered indicative of an inadequate adrenal response to the stress of the infection. An extremely acute meningococcic infection has been ascribed to an infectious factor and to a general collapse; the first of these can now be overcome with antibiotics and chemotherapy. Until recently these patients died from the shock that was brought about by the severe alterations of the adrenal cortex that resulted in acute insufficiency of the adrenal gland. An adequate replacement therapy was needed, which combined with the antibiotic therapy would keep the patient alive until the antibiotic produced its effect. The authors used cortisone in these two patients. They gave it in doses of 50 mg. for six days and 25 mg. for four days to one patient and in doses of 50 mg. for the first two days, 37.5 mg. the third day, and 25 mg. the fourth day to the second patient. In both the severe initial state of collapse regressed within 24 hours, fever disappeared, the number of eosinophils dropped, the general condition improved, and the children recovered in the normal space of time. In the other six patients the infection was moderate and was associated with meningitis. In them the eosinophil values ranged from 5.5 to none per cubic millimeter, indicating an adequate adrenal response to the stress of the infection. Cortisone was given also to these children in doses of 25 and 50 mg. for a few days. The initial toxic state and hemorrhagic signs regressed, but the therapy did not produce a positive or negative effect on the course and duration of meningitis. The count of the circulating eosinophils in case of meningococcic infection is valuable in that it indicates the functioning condition of the adrenal and whether the infection is extremely acute or only moderate. Cortisone combined with antibiotic therapy is valuable in the case of extremely acute meningococcic infections, and it produces good effects also in the case of infections of average severity.

The Question of Endocrine Disturbances During Treatment with Isonicotinic Acid Hydrazid. A. Beyer. Ztschr. ges. inn. Med. **9**:909-911 (Sept. 15) 1954 (In German) [Leipzig, Germany].

Beyer presents the case of a man, aged 24, in whom an attack of pleurisy was followed by a new tuberculous dissemination. The patient was given daily 7 tablets (equivalent to 700 mg.) of isonicotinic acid hydrazid (isoniazid). The total dose was 400 tablets. The patient's weight at the onset was 77 kg. (170 lb.). During and immediately after treatment he gained a total of 11 kg. (23 lb.). He observed the appearance of purplish streaks on the lower abdomen and a decrease in potency. Examination revealed increased fat deposits on the trunk, the typical moon-face, and a series of purple striae on the lower abdomen. The blood pressure was slightly increased. The patient had the typical signs of adrenal cortical hyperfunction (Cushing's syndrome). Beyer mentions other authors who had observed patients with signs suggestive of adrenal cortical hyperfunction during treatment with isoniazid. Similar observations have been reported during treatment with Amithiozone (TBI). The pathogenesis of this form of adrenal cortical hyperfunction is difficult to explain. One investigator observed an accumulation of isoniazid in the incretory organs, and particularly in the hypophysis. This might suggest that the reaction-chain: increased corticotropin production-increased function of the adrenal cortex might produce a cortisone-like effect, but this would rather activate than suppress the tuberculous process. Formation of striae likewise cannot be regarded as proof of a hypophysial disturbance, because together with other signs of

adrenal cortical hyperfunction it is likewise observed during treatment with cortisone. Thus it cannot be definitely decided whether isoniazid acts on the hypophysis, the adrenal cortex, or on both, or whether the primary lesion is produced in the diencephalon. The prognosis of this form of adrenal cortical hyperfunction is favorable. Nine months after cessation of the isoniazid therapy the symptoms showed a good tendency to regress.

Temporary Reduction of the Intestinal Flora as Preparatory Treatment for Surgical Intervention on the Colon. F. Andina and O. Allemann. Chirurg **26**:12-15 (Jan.) 1955 (In German) [Berlin, Germany].

Andina and Allemann emphasize that antibiotics that are resorbed from the gastrointestinal mucosa should not be used in the preoperative antibacterial treatment directed at the temporary reduction of the intestinal flora, because their passage into the blood is undesirable. Drugs that are not easily resorbed and consequently exert a local effect on the intestine only must have preference. Two or more drugs should be combined, so that the spontaneous regeneration of the intestinal flora may occur before the rise of dangerous antagonists. This can be achieved effectively by the synergism of neomycin and sulfonamide compounds. Prophylactic addition of a fungicide may prevent the antagonistically conditioned infection with Candida albicans. These concepts induced the authors to give a therapeutic trial to "Intest-Steril," a preparation one tablet of which consists of 166 mg. of neomycin sulfate, 126 mg. of phthalylsulfathiazole, 126 mg. of formaldehydesulfathiazole, 110 mg. of methyl paraoxybenzoate, and 56 mg. of propylparaoxybenzoate. One hundred eight patients were placed for three to four days on a diet consisting of tea, toast with butter, broth thickened with oatmeal, apple sauce, and fruit juices to which a vitamin B complex preparation and vitamin K were added. On the first day the patients were given three to four times 2 tablets of "Intest-Steril" with tea or milk; on the second day, three times 2 tablets of "Inter-Steril" with tea or milk, and on the third day 1 to 2 tablets. Before the institution of the treatment and on the second and third day of the treatment bacteriological examination was carried out on the feces of the patients who were subjected to surgical intervention on the fourth or fifth day. Results of the bacteriological examination in 60 patients were as follows. Before the institution of the treatment with "Intest-Steril" enterococci were observed in the feces of all the patients, Escherichia coli in 40, Proteus in 40, Pseudomonas aeruginosa in 10, fungi in 22, and anaerobia in 50. After three days of treatment none of these bacteria were found in the feces. Although the number of patients was small, the surprising reliability of the preparation in producing sterilization of the feces was notable. Undesirable side-effects were not observed.

Anemia in Lead Poisoning and Vitamin B_{12}. H. Kleinsorge, E. Morigerowski and K. Rösner. Ztschr. ges. inn. Med. **9**:903-906 (Sept. 15) 1954 (In German) [Leipzig, Germany].

Kleinsorge and associates studied the bone marrow and blood in rabbits that had been rendered anemic by injection of an aqueous solution of lead acetate into the ear vein on three successive days. Since difficulties had been encountered in obtaining marrow specimens from the vertebral bodies of rabbits, the authors tried a new method, in which they puncture the crest of the ilium. They explain that if the rabbit is placed in a certain sitting posture, the crest of the ilium is readily accessible. They found that the administration of vitamin B_{12}, either simultaneously with or immediately after the lead dosage, resulted in a much more rapid recovery from the anemia. Stimulation of the regenerative power of the bone marrow was demonstrated to be the cause of this more rapid recovery. Vitamin B_{12} also prevented deterioration of the general condition of the rabbits with lead poisoning. Furthermore, when lead was given simultaneously with vitamin B_{12}, the development of basophilic stippling of the erythrocytes was prevented. The authors feel that either normal maturation is stimulated so that supposedly immature erythrocytes with basophil stippling are not flushed out, or a pathological process of ripening (perhaps resulting from the inhibition of the nucleic acid metabolism by lead?) is normalized, because vitamin B_{12}, an important factor in the nucleic acid metabolism, is present in large quantities.

RADIOLOGY

Treatment of the Carotid Sinus Syndrome by Irradiation. H. P. Greeley, M. I. Smedal and W. Most. New England J. Med. **252**:91-94 (Jan. 20) 1955 [Boston].

The important sign of the carotid sinus syndrome is spontaneous syncope; diagnosis of the syndrome is made by reproducing the symptoms on carotid sinus pressure, but the elicitation of these symptoms in a person in whom they do not occur spontaneously does not warrant the diagnosis of carotid sinus syndrome. An aura may precede the attack. Convulsions may occur during attack. The attack usually lasts no more than a few seconds, with complete return to consciousness. The patient is often unaware of the whole episode. In a series of 52 patients with the syndrome, x-ray therapy as the sole therapeutic agent effected a complete remission in 58%. An additional 12% were moderately benefited. A remission of over 14 years is reported. The irradiation technique is as follows: 200 to 220 kv. with a 2-mm. filter of copper and a 1-mm. filter of aluminum, a 50-cm. target-skin distance, 200 r (measured in air), and a 5-cm. square portal. Two or three treatments are given, preferably on alternate days. The total dose to the affected sinus area is 500 r if unilateral and 400 r if bilateral (measured in air). The condition is usually unilateral. Failure to obtain benefit from irradiation may mean that there is serious, unrecognized coronary sclerosis. The mechanism of relief by irradiation is not known; it may be depression of nerve endings. This treatment has the advantages of being harmless, acting promptly (in a few days or hours) when it is successful, being inexpensive, and being of value in all types of the syndrome, whether vagal, depressor, cerebral, or mixed.

ANESTHESIA

Singultus in Patients During and After Anesthesia. H. C. Voorhoeve. Nederl. tijdschr. geneesk. **98**:3289-3294 (Nov. 13) 1954 (In Dutch) [Haarlem, Netherlands].

Voorhoeve defines singultus or hiccup as an involuntary contraction of the diaphragm that causes a sudden inspiration that is interrupted by closure of the glottis producing the characteristic sound. He comments on the respiratory center in the brain and on how hiccup may be induced not only by disturbances in the central nervous system or by anesthesia but also by mediastinal tumors, pericarditis, gastritis, dilatation of the stomach, pancreatitis, peritonitis, etc. Treatments included those in which the point of attack is not known, such as aminopyrine, quinine, quinidine and tincture of valerian; those that influence the entire reflex pathway, namely, pentothal, pethidine, cyclopropane; those that affect the efferent pathways, such as pressure on the phrenic nerve, blocking of the nerve with solution of procaine hydrochloride or of alcohol, phrenicotomy, injection of curare, or of succinylcholine; those that influence the afferent pathways, namely, intravenous injection of procaine amide, administration of methonium salts, or induction of artificial hibernation; and substances that exert a stimulating effect on the respiratory center. These are carbon dioxide, amyl nitrite, and particularly desoxyephedrine (pervitin). The author was particularly impressed by the effect of this last drug. He mentions Fajardo's successful use of this drug in 16 cases in which hiccup had begun in the course of gastric resection or cholecystectomy. He himself resorted to the intravenous administration of desoxyephedrine in eight patients in whom hiccup had developed during operation. In all eight patients the hiccups ceased within two minutes after the injection of the drug. He presents the history of a woman in whom hiccup had persisted uninterruptedly for six days and nights. After the intravenous injection of 10 mg. of desoxyephedrine, the hiccup ceased but recurred about 18 hours later; after another intravenous injection of the drug the hiccup disappeared.

BOOK REVIEWS

Clinical Approach to Jaundice. By Leon Schiff, M.D., Ph.D., Professor of Clinical Medicine, Department of Internal Medicine, University of Cincinnati College of Medicine, Cincinnati. Publication number 202, American Lecture Series, monograph in American Lectures in Abdominal Viscera. Edited by Lester R. Dragstedt, M.D., Chairman, Department of Surgery, University of Chicago, School of Medicine, Chicago. Cloth. $3.75. Pp. 113, with 52 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, Canada, 1954.

In this small monograph the author has attempted to clarify the diagnostic information that the clinician may gather during the study of a patient with jaundice. He has divided the book into four sections, each representing a different method of approach to this difficult problem: (1) clinical examination; (2) laboratory tests; (3) roentgen examination; and (4) needle biopsy of the liver. He points out that the history and physical examination alone provide the diagnosis in 60 to 70% of patients with jaundice, and the author draws heavily on his own clinical observations. He also discusses certain features in the history and physical examination that have been stressed by other authorities in the field. The section on laboratory tests is nontechnical, and the author points out many of the pitfalls in the interpretation of some of the currently used liver function tests. He discusses only the tests that are used in his laboratory. The section on the x-ray examination consists mainly of reproductions of roentgenograms and a general description of the clinical usefulness of the x-ray in the differential diagnosis of jaundice. In the section on the needle biopsy of the liver the author gives a detailed description of the technique that is used in his hospital and has some excellent reproductions of typical histological sections that may be obtained by this technique. He also gives an excellent detailed description of the various microscopic changes found in various hepatic disorders.

He makes no attempt to discuss the classification of jaundice nor does he describe any of the diseases or pathological conditions that cause it. Rather, he confines himself to general discussion and interpretation of the various clinical and laboratory data that should be obtained in the study of a patient with jaundice. The volume is well printed, and the illustrations are excellent. This book is recommended to the medical student as his first introduction to this topic and also to the clinician who wishes a basic review on the clinical approach to the patient with jaundice.

Fluid Balance in Surgical Practice. By L. P. Le Quesne, M.A., B.M., B.Ch., Assistant Director, Department of Surgical Studies, Middlesex Hospital, London, England. Cloth. $3.50. Pp. 130, with 41 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1954.

This small volume is based on the Moynihan prize for 1953 and appears to be the first recent monograph on the subject of fluid balance by an English surgeon. An excellent monograph on water and salt depletion by H. L. Marriott, an English physician, was published in 1950. As in all discussions on water and electrolyte, theory and practice are difficult to unify. In this monograph the case reports and experiences of the author are most valuable and informative, whereas their correlation with theory leaves much to be desired. This is perhaps best illustrated by the discussion on basic water and electrolyte needs of the well-nourished patient after uncomplicated abdominal operations. This occupies about 60% of the actual text and contains valuable and original observations based on urinary, blood, and other measurements in 24 patients personally studied and given a minimum of 4 liters of water, 150 gm. of glucose, and 10 gm. of sodium chloride per day. On this intake there was always a weight gain on the day of operation, which in 5 of 10 patients exceeded 2 kg. This phenomenon was called "primary water retention." It would be just as accurate and perhaps more useful practically to describe the findings as an example of excessive water administration. The author recognized such a hazard a little later when he stated that during the first 48 hours after operation "the main danger is that of overloading with water," yet on the very next page he considered the recommendation of a 2 liter daily intake as "overinfluenced by the fear of excessive administration." The author estimates the basic needs after operation as 3 liters of water, 150 gm. of glucose, 4.5 gm. of sodium chloride, and 6 gm. of potassium chloride per day, an intake that was then given in a second group of patients. It would have been interesting to compare the data in these cases with those receiving 4 liters or more; but only one example is given in which there was no weight gain on the day of operation, although the statement is made that these patients all had "excellent results." The theoretical basis for giving the 3 liters was simple: 1.5 liters for urine, plus 1.5 liters for insensible losses, amounts that would be considered excessive by many surgeons in this country. Moreover, this theoretical calculation did not take into consideration the endogenous supply of 500 ml. of water resulting from tissue breakdown, although the author mentions this factor elsewhere.

These theoretical considerations of basic water and electrolyte needs are of great practical importance because in this country at least there is a disturbing tendency for the surgeon (or usually the intern or nurse) to administer excessive amounts of water and salt during an uncomplicated postoperative course. This is particularly true in infants. Many surgeons would consider 75 ml. per kilogram of body weight closer to the parenteral water needs following operation in early infancy than the 100 to 150 ml. per kilogram that is usually given. The latter estimate is based largely on the water content of the average oral intake of milk or formula under normal conditions. Le Quesne recommends the latter rather than the former figure.

Of special interest are the data on three patients given 6 gm. of potassium chloride on each (except for the first) postoperative day. This is a larger intake than most surgeons would recommend in this country, yet it apparently caused no harm and resulted in an approximate balance in each case. The author rightly emphasizes bedside rather than laboratory determinations and simple rather than complicated guides to therapy. The reader will find the text easy to follow and understand. An exception was the alternating but only occasional simultaneous use of both milliliter and ounce for volume and of both kilogram and pound for body weight. It would have been preferable to have used the metric system throughout.

Surgical Treatment of Cancer of the Cervix. Edited by Joe V. Meigs, M.D., Clinical Professor of Gynecology, Harvard Medical School, Boston. Cloth. $12. Pp. 462, with illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1954.

The first three chapters of this book discuss the anatomy, blood vessels, lymph nodes, and channels of the pelvis, and the sympathetic and parasympathetic nerves of the ureters and bladder. An accurate and extensive knowledge of this anatomy and particularly the cleavage planes is of primary importance in obtaining the best surgical results. The evaluation of radiation versus operation in treatment of cancer of the cervix has been made in a lucid and concise manner. The author believes that the two methods should be used, but that the individual circumstances should decide the choice of treatment. He is not in favor of combining the two types of therapy. As an open-minded clinician he discusses the unknown factors of the lymph system and the questionable results of removal of the nodes. The pros and cons of evisceration procedures are squarely faced and evaluated. Dr. Meigs states that one of the objectives of this book is "to acquaint surgeons and gynecologists with all the major surgical approaches" in treating carcinoma of the cervix. This is done admirably in the chapters that deal with operative procedures. The techniques are described in detail and

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are amply illustrated. Dr. Meigs has compiled an outstanding book at a time when there is much controversy concerning radicalism versus conservatism; radiation versus operation. This book can be recommended wholeheartedly to anyone interested in cancer of the cervix.

Human Limbs and Their Substitutes: Presenting Results of Engineering and Medical Studies of the Human Extremities and Application of the Data to the Design and Fitting of Artificial Limbs and to the Care and Training of Amputees. By Paul E. Klopsteg, Ph.D., Sc.d., Philip D. Wilson, M.D., et al. Prepared under sponsorship of Advisory Committee on Artificial Limbs, National Academy of Sciences, National Research Council, in summary and correlation of research program for Department of Medicine and Surgery, U. S. Veterans Administration, and for Office of Surgeon General, Department of the Army. Cloth. $12. Pp. 844, with illustrations. McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E.C.4, England, 1954.

This is one of the best books published on prostheses. There has been a great need for an adequate description of prosthetic limbs and particularly one that is complete and up-to-date. This book satisfies this requirement. The general outline of the book is exceedingly well done. Practically each chapter is a monograph within itself, and the detailed drawings and photographs add much to the value of the volume. This book is timely, particularly in its first half, which deals with the newer concept of upper extremity prostheses. Prior to 10 years ago upper extremity prostheses were of little functional value. Through the research work conducted by the National Research Council, the Committee on Artificial Limbs, the Veterans Administration, and the University of California at Los Angeles, to mention only a few, the upper extremity prosthetic program has been given great impetus. The value of teamwork in the approach to the upper extremity problem has been of inestimable value. The chapter on biomechanics reflects the great amount of work that has gone into the preparation of a book such as this. In the section on lower extremities all of the newer aids and mechanical devices are well illustrated and their indications and contraindications given. The psychological aspect of the amputee, be it upper or lower extremity, has been investigated extensively, and an accurate guide to the treatment of this phase is presented. While the book is rather large it serves as an excellent reference book and should be a valuable aid to anyone working with amputees. It should be in every hospital library, particularly hospitals that include resident training programs.

The Skin: A Clinicopathologic Treatise. By Arthur C. Allen, M.D., Associate Pathologist, Memorial Hospital, New York City. Cloth. $25. Pp. 1048, with 496 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1954.

It is a hazardous undertaking for one who is not a dermatologist to write a book on the skin, for, in general, attempts to bridge gaps between specialties produce unsatisfactory results. This book by a general pathologist comes close to being the rare exception to that rule. Designed primarily to stimulate the interest of fellow pathologists in the field of cutaneous diseases and to reduce the barriers between dermatology and other disciplines, it accomplishes its aim admirably by the use of a well-selected group of photographs, a clear concise text, and effective grouping of diseases with special emphasis on points of differential diagnosis. Nearly one-third of the book is devoted to tumors and the remainder includes, along with the common diseases, many rare diseases and syndromes, exanthems, an interesting list of dermatological eponyms, and an excellent chapter on embryology, anatomy, and physiology. The author has omitted minutiae in descriptions and details of treatment that standard textbooks of dermatology usually and understandably do contain. Because of the excellence of the book, one may overlook relatively unimportant errors and controversial items, such as that pityriasis rosea may be initiated by new clothes and that it is histologically identifiable, the illustration of keloid as a result of radiation therapy for acne, and the categorical inclusion of lichen simplex chronicus with the psychoneurotic diseases.

The book benefits from a single authorship, not only by a uniformity of writing style and a presentation that reflects a stimulating and effective teacher, but also by the inclusion of personal stands, especially those few that sometimes run against the current, e. g., "There is adequate reason to conclude that neither lupus erythematosus nor dermatomyositis is a diffuse vascular disease or a generalized disease of collagen." The section on malignant melanomas is especially interesting. The illustrations alone are sufficient reasons for owning the book. The innumerable, large, clear, well-selected and functionally grouped clinical photographs and photomicrographs are printed on heavy stock to good advantage. There is a large number of current references, and the book is fully indexed. The pages are large, and the book weighs almost 10 pounds, but it is not meant to be carried about. Because of its objectivity and refreshing approach to the subject, it is highly recommended.

Curriculum Study in Basic Nursing Education. By Ole Sand. Basic nursing education curriculum study series, volume I, under editorship of Ole Sand. Cloth. $3.75. Pp. 225. G. P. Putnam's Sons, 210 Madison Ave., New York 16, 1955.

This little volume is a progress report of a five year curriculum research project in basic nursing education now in its third year at the University of Washington school of nursing. The study was undertaken as a result of two important surveys on nursing in the state of Washington. A survey of the nursing needs and resources was completed in 1950. A second survey, completed in 1951, directed its attention toward the improvement of nursing and recommended that the University of Washington school of nursing exert leadership in strengthening diploma programs in the state and develop a research program in nursing education. The current studies are being financed by grants from the National Institutes of Health (Public Health Service) and the Commonwealth Fund.

Although the material is primarily addressed to faculty members in schools of nursing, there is much information that should be helpful to faculties of other professional schools or areas of university discipline. The author indicates that efforts at curricular improvements must be focused primarily on sharpening the understanding of the faculty concerning the objectives they are seeking so as to cooperatively direct efforts to these important ends. The various sections of the volume deal with objectives, philosophy, and theory of learning; selection and organization of learning experiences in clinical areas; relation of general and professional education; relation of social and natural sciences and clinical nursing; and cooperative faculty action. It is a well-written, attention-holding volume deserving of study and review by those concerned with the problems of intelligent curricular planning, regardless of the field of education in which the reader may be engaged.

Human Factors in Highway Transport Safety. By Ross A. McFarland, Ph.D., Associate Professor of Industrial Hygiene, Harvard University School of Public Health, Boston, and Alfred L. Moseley, M.A., Research Associate in Industrial Hygiene. Paper, loose-leaf. [Limited supply available.] Pp. 295, with illustrations. Department of Industrial Hygiene, Harvard School of Public Health, 695 Huntington Ave., Boston, 1954.

The research team approach to one of the serious problems of our time has paid off handsomely in this volume. Specialists in the fields of medicine, anthropology, physiology, engineering, psychology, and psychiatry collaborated to produce this critical examination of the many factors within and around "John Doe" as a truck or bus driver that have a bearing on his chance of being involved in traffic accidents. The subject is handled in highly satisfactory style. Each chapter presents a comprehensive yet compact review of the various elements involved, without the usual minutiae characteristic of so many research reports.

Although our national traffic accident record is appalling and shameful, there is not much evidence that the generalized safety campaigns are having any noticeable effect on the total situation. Fortunately, the operators of fleets of trucks or buses are in a good position to accomplish positive results through the proved techniques of organization, supervision, selection, and training of personnel. This book points out the shortcomings of current practices in driver hiring, testing, and examination. It considers procedures for detecting the accident repeater; health maintenance, including the influence of tobacco and amphetamine (Benzedrine); fatigue (and hallucinations); driver age; and the relationship of the various comfort factors.

Many owners of truck fleets may be amazed to learn that the much-vaunted engineering talent of the automotive engineers and designers has often neglected the most important feature of the beautiful, colorful, chrome-trimmed, super-powered giant that traverses the highways, namely, the driver. Frequently scant attention is paid to the bodily proportions of the average truck driver and his job-motion activities and needs. Too little attention is paid to functional factors in the design of cabs, seats, windows, and the placement of pedals, levers, buttons, etc. The importance of these factors as possible contributing causes of accidents is brought out in detail in an important part of the book. There is also a comprehensive delineation of the organization and functions of the medical program in the highway transport industry. Undoubtedly, this is a fertile field for preventive medicine. While the book should be of special value in the commercial vehicle field, it is recommended to all who have any interest in the automobile safety problem.

British Pharmaceutical Codex 1954. Published by direction of Council of Pharmaceutical Society of Great Britain. Cloth. £3.3s. Pp. 1340; xxxii. The Pharmaceutical Press, 17 Bloomsbury Sq., London, W.C.1, England, 1954.

The latest edition of the British Pharmacopoeia made the 1949 edition of the Codex obsolete; hence this new edition. As in the past, it includes many of the nonofficial, as well as the official, drugs used in the British Empire. Despite the fact that 69 new substances and 84 new formulations were added, so many of the less-used drugs and formulations were dropped that the book is 200 pages shorter than its predecessor. The work is divided into the following main sections: general monographs (on active ingredients); antiserums, vaccines, and related substances; preparations of human blood; formulary (giving directions for the extemporaneous compounding of such drugs as are sold in bulk); appendixes (covering reagents and tests); and an index. While much of the material concerns pharmacists, e. g., solubility, purity, and compatibility, physicians will have use for the short, critical paragraphs on pharmacology and therapeutics, the lists and descriptions of dosage forms in which the drugs are prescribed, and the symptoms and treatment of poisoning from the more toxic drugs. In a separate 10-page booklet are listed the brand names under which various drugs contained in the "Codex" are marketed in the British Empire. This is the first edition of the "Codex" to use English names for the drugs as the main ones. Latin names are retained as synonyms. The paper, printing, and binding are of high quality.

Healthier Living: A Text in Personal and Community Health. By Justus J. Schifferes, Ph.D., Director, Health Education Council. Introduction by John E. Sawhill, M.D., University Physician, New York University, New York. Health Education Council book. Cloth. $6.75. Pp. 928, with illustrations by Louise Bush, Ph.D., John Wiley & Sons, Inc., 440 Fourth Ave., New York 16; Chapman & Hall, Ltd., 37-39 Essex St., Strand, London, W.C.2, England, 1954.

This textbook is the author's attempt to meet the objectives for a basic college course in personal and community health stated by the Third National Conference on Health in Colleges in May, 1947. Its chapters are grouped according to subject matter. Each is followed by a bibliography and several discussion questions to stimulate review and understanding. Most of the material expected in a college health textbook is here, but the emphasis is definitely on education for family living, including much material on growth and development, reproduction, sex adjustment, love, and marriage. Mental health is also emphasized, even to suggestions on the development of a satisfying personal philosophy. The standard items on personal health are interestingly covered, and community health is considered to be the sum of and extension of the personal health of individuals. There is an excellent discussion of the personal and family relations with physicians, both in general and in special practice. The physician's code of ethics, the devices used in diagnosis and treatment, the dangers of self-treatment, the hazards of fads and quackery, and the economics of medical and hospital care are well covered. The college student is approached as an adult with adult problems, but in a light conversational tone and a minimum of technical terms. This volume could serve not only as a textbook or reference for class use but as a reference in the homes of noncollege families.

Essentials of Medicine: The Art and Science of Medical Nursing. By Charles Phillips Emerson, Jr., A.B., M.D., Associate Professor of Medicine, Boston University School of Medicine, Boston, and Jane Sherburn Bragdon, R.N., B.S., Associate Director, School of Nursing, Massachusetts Memorial Hospitals, Boston. Seventeenth edition. Cloth. $4.75. Pp. 922, with 268 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; 2083 Guy St., Montreal, Canada, 1955.

This book is intended for nurses and, as such, has become well known by nurses for reference and teaching purposes. There will be times when the teacher will need to supplement this material, not only by his or her own experience but also by reference to more complete treatises. For one interested in a briefly but clearly presented roundup of the essentials of medical nursing, however, this book deserves the popularity it has achieved.

The Principles and Practice of Medicine: A Textbook for Students and Doctors. By L. S. P. Davidson, B.A., M.D., F.R.C.P., Physician to H.M. the Queen in Scotland, and staff of Department of Medicine, University of Edinburgh, and associated clinical units. Second edition. Cloth. $7. Pp. 1036, with 80 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Pl., Edinburgh 1, Scotland, 1954.

There are some who insist that it is impossible to bring out today a book in which therapeutics is included without the risk of its being out of date before it is ready for the reader. Medical discoveries are announced more rapidly than it is possible for printers to move. Nevertheless, there are fundamental concepts that are sound, and a basic knowledge is sufficient to permit the issuance of textbooks with less fear than might be imagined. Davidson's book is such a volume. It is sufficiently small to be handy and yet large enough to be helpful and informative for the medical student and average practicing physician. It has an English background, but this does not hinder its usefulness elsewhere in the world, as medical knowledge is shared much more quickly today than a decade or two ago. Furthermore, the list of contributors to this book is impressive, and their knowledge, along with the author's, has permitted the development of a book that should be satisfying to the average reader. The contents are classified according to diseases affecting the systems of the body, and here and there are interspersed figures and plates—some of them in color—that emphasize important points in the chapters. It is a book that can be read with satisfaction by those who are seeking the essentials and not all the details of the major medical problems.

Recent Developments in Cell Physiology. Edited by J. A. Kitching. Proceedings of seventh symposium of Colston Research Society held in University of Bristol, March 29th-April 1st, 1954. Cloth. $6.50. Pp. 206, with illustrations. Academic Press, Inc., 125 E. 23rd St., New York 10; Butterworth's Scientific Publications, 88 Kingsway, London, W.C.2, England, 1954.

This book consists of 15 contributions by investigators from Great Britain, Denmark, and Belgium. They should interest biologists concerned with the physiology of the cell. Specialists in the several topics covered will find more technical accounts by many of the same authors in other recent symposiums. Almost all of the papers are introduced for the orientation of the general physiologist, and the presentations are individually excellent. Stimulating hypotheses are freely presented, thus successfully filling a prime but often neglected function of a published symposium. Danielli, Koch, Ussing, and Keynes discuss permeability and membrane structure emphasizing active transport; metabolism of the cell is presented by Yemm with regard to synthesis of amino acids in plants, by Klenow on the biosynthesis of pentoses, by Hoff-Jørgensen on the nucleic acid content of certain eggs, and by Brachet on nuclear control of enzymes; Waddington reviews physiological mechanisms in early development, and Brøndsted presents further experiments and theory on planarian regeneration. The relation of temperature shifts to the control of cell division is discussed by Zeuthen and Sherbaum for the ciliate Tetrahymena and by Maaløe and Lark for bacterial populations. Other factors controlling cell division are proposed by Swann. Westergaard and Hirsh deal with differentiation in Neurospora, and Kitching discusses the origin of suction in Suctoria. Editor and publisher are to be complimented on the speed of publication of this volume with so high a proportion of genuinely recent developments. The volume should have a wider appeal than the heterogeneity of subjects would at first indicate.

QUERIES AND MINOR NOTES

UTERINE SUSPENSION

TO THE EDITOR:—*Please comment on the following statement: "Leading gynecologists have recently deplored the performance of 'uterine suspension' on the grounds that it is ineffectual in a great many cases of retroversion."* *M.D., Illinois.*

ANSWER.—As knowledge increases on the subject of retroposition of the uterus, fewer and fewer suspensions for simple retroversion are being done. If one contemplates operating on a simple retroversion, the use of the Smith or Hodge pessary is recommended for a period of two months as a therapeutic test. If the symptoms are relieved, then an appropriate procedure is done. In simple retroversion the organ is of normal size, with no descensus and only backward displacement. Whenever the bladder becomes filled such a simple retroversion occurs, and certainly it cannot be considered pathological. In the past, many neurotic patients with dysmenorrhea with uteri of this type were operated on to no avail. Patients with retroversion of the uterus resulting from difficult childbirth, associated with uterine descensus and hypertrophy, laceration of the cervix, cystocele, and rectocele, are greatly benefited by suspension and reparative operations of the associated lesions. Should a nonsymptomatic retroversion, resulting from childbirth, be operated on? Some believe there is associated ovarian enlargement due to congestion and cyst formation that eventually is detrimental to normal ovarian function, and on this reasoning a suspension of the uterus and ovary is advocated. This seems somewhat debatable.

CORONARY ARTERY DISEASE

TO THE EDITOR:—*Reviewing medical reports of employees of a brewing industry in this locality, I noticed over 5% of brewers, bottlers, and truck drivers were suffering from coronary artery disease. Their average age is 45 to 55 years, with an occasional person aged 25 to 35. However, this disease is uncommon among the clerical and the executive staff. Is this high incidence peculiar only to the brewing industry?* *M.D., New Jersey.*

ANSWER.—There is no conclusive evidence of a significant correlation between the occurrence of coronary artery disease and occupation. The discrepancy in the incidence of this disease in the manual trades and the office positions in one brewing industry plant is thus unusual. This difference may represent a statistical artefact due to the nature and volume of the population sampled. The body type in the two groups could be a factor. Coronary artery disease is more prevalent in the muscular, stocky habitus than in the slender, asthenic body form. A careful analysis of such factors is presented in a recent study (Gertler, M. M., and White, P. D.: Coronary Heart Disease in Young Adults, Cambridge, Mass., Harvard University Press [Commonwealth Fund], 1954). The over-all incidence of coronary artery disease in the group in question is not unusual. Probably the majority of men over 45 years of age show some degree of atheromatous change in the coronary arteries at postmortem examination. The extent of the clinical disease depends on the criteria for diagnosis, i. e., angina pectoris, myocardial infarction, or electrocardiographic patterns suggesting coronary artery disease. If all such criteria were used in the analysis in question, the incidence of the disease would not be out of line with that present in other industries. Stout thus summarizes the matter: "The mass of evidence indicates that work and exercise do not precipitate coronary thrombosis, coronary occlusion, or myocardial infarction."

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

GASTROCOLIC FISTULA

TO THE EDITOR:—*Can you give me any statistics on percentage of gastrocolic fistula following gastroenterostomy and following gastric resection?* *W. J. Tucker, M.D., Ashland, Wis.*

ANSWER.—Accurate statistics concerning the incidence of gastrocolic fistula following gastroenterostomy and gastric resection are not available. Gastrojejunocolic fistula is almost always a complication of marginal or gastrojejunal ulcer and, accordingly, occurs in some patients when gastrojejunostomy or partial gastric resection has been done in the treatment of duodenal ulcer. Stomal ulcers rarely occur when these operations are performed for gastric ulcer or gastric carcinoma. Gastrojejunocolic fistula has been estimated to occur in from 5 to 25% of patients with gastrojejunal ulcers (Wright: 8.7%; Judd and Hoerner: 8.7%; Ranson: 17%; Benedict; 23.8%; Verbruggen: 11.3%; Walters and Claggett: 13.6%). According to Lahey, the usual estimate of one gastrojejunocolic fistula following every 100 gastrojejunostomies is probably an exaggeration of the true frequency of the disease.

BROMIDES OR CHLORAL HYDRATE FOR MENTAL PATIENTS

TO THE EDITOR:—*Is it bad practice to use 1 oz. (about 30 ml.) of three bromides elixir (triple bromide) three or four times per day for six days only or 1 or 2 teaspoons (about 4 to 10 ml.) of bromide and chloral hydrate one or two times per day when necessary for the treatment of noisy, nervous, disturbed mental patients? Please discuss these two medicaments and their value when not given over too long a period.*

Martha Moore, M.D., North Madison, Ind.

ANSWER.—Bromides in the amount stated may lead to chronic bromide intoxication or bromism. Two to 10% of patients admitted to psychopathic hospitals are found to be suffering from some degree of bromide intoxication. The additional use of bromides will increase the mental symptoms as intoxication progresses. Some patients show toxic symptoms at levels of less than 100 mg. per 100 cc., as there is no absolute correlation between the severity of the poisoning and the level of bromides in the blood. Chloral hydrate is described by Goodman and Gilman (The Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941) as one of the cheapest and most effective hypnotics. In its presence the urine may give a false positive reaction for sugar. A death has been reported to occur from as little as 4 gm. of chloral hydrate. Care should be exercised in not giving more than 2 gm. of the drug in a single dose. Chloral hydrate is a more rapidly acting sedative than are bromides and has less after-effects.

POLLEN IN HAWAII AND ALASKA

TO THE EDITOR:—*A 9-year-old child who has severe pollen asthma may go to Hawaii or Alaska. Please let me know the merits of these locations.* *M.D., Virginia.*

ANSWER.—The correspondent does not indicate which pollen or pollens are active in the case of the 9-year-old child, but it is assumed that ragweed (Ambrosia) is involved. An examination of the five large islands of the Hawaiian group in 1948 revealed only a trace of common ragweed in one area, namely, the north end of the large island, Hawaii. Here along the main road south of Waimea (Kamuela) for a distance of two miles a few poorly developed specimens were seen. Seeds evidently had been brought into this area in Army trucks used in maneuvers during the war. It is doubtful that the plants are surviving today. In the central valley of Oahu there is a large area between Pearl Harbor and Scofield Barracks where false ragweed (Franseria strigulosa) is abundant along roadsides and in waste places. The period of pollination of these perennial plants seems to be more

or less continuous, for in September there were plants in all stages of development. Apparently the only reason why ragweed pollen from this area does not reach the city of Honolulu is that the prevailing winds carry it in the opposite direction. Reports of atmospheric tests made in the city have never mentioned ragweed pollen. Goosefoots (Chenopodium) and amaranths are present in cultivated ground, but the acreage of such weeds is negligible. Sages (Artemisia) are present in the hills, but only in small amounts. Grass pollens are, of course, unavoidable anywhere in the tropics. Hawaii is no exception. Bermuda grass (Cynodon dactylon) is present. Most of the local tropical trees and shrubs are insect-pollinated. Wind-pollinated species are almost entirely absent.

Again assuming that ragweed is the only active pollen factor in this case, Alaska can be highly recommended. Atmospheric tests in Juneau, Fairbanks, and Nome gave these places a perfect ragweed rating. It can be safely assumed that other communities are likewise free from the pollen, although there is a trace of one insignificant species of ragweed (Franseria bipinnatifida) growing in the sand along the shore in some parts, probably the southern part, of Alaska. Grasses are known to be a source of trouble to grass-sensitive persons in southern Alaska.

REACTION FOLLOWING THIAMINE BY VEIN

To the Editor:—*Since thiamine (vitamin B_1) has been known to cause death when injected intravenously, the hospital with which I am connected will not permit it to be given by this route. Recently I had occasion to give ascorbic acid (vitamin C) intravenously and an immediate headache, sweat, and near collapse ensued. This occurred twice, so I discontinued its use this way. I have been giving thiamine subcutaneously, and on two occasions an immediate loss of equilibrium with a momentary collapse ensued. All of these preparations were preserved with chlorobutanol, which I believe is related to chloroform and carbon tetrachloride and might be a dangerous chemical to inject. Would it account for these episodes rather than allergy?*

Monroe B. Kunstler, M.D., New York.

Answer.—Chlorobutanol, usually in concentrations of 0.5%, has been used extensively as a preservative of certain injectable medicaments for many years, but no reports are found that cast suspicion on this compound as a possible cause of toxic or untoward reactions following the injection of therapeutic agents. New and Nonofficial Remedies (1954, p. 564) points out that intravenous administration of thiamine hydrochloride is neither necessary nor desirable and that injection of large doses of highly potent solutions may cause anaphylactic shock.

TRAUMATIC HEMARTHROSIS OF SCAPULOHUMERAL ARTICULATION

To the Editor:—*What is the best treatment for traumatic hemarthrosis of the scapulohumeral articulation? Is early mobilization better than prolonged immobilization? Can a certain degree of ankylosis that lasts for several weeks or months be produced by immobilization?*

M.D., Belgian Congo.

Answer.—In the treatment of traumatic hemarthrosis of the scapulohumeral articulation, it is advised that ice compresses and immobilization be used only during the initial period of acute trauma and pain. This period should not last over 24 hours, at the end of which time further bleeding or the danger of bleeding recurring from movement should have passed. Following this the use of radiant heat, preferably infrared radiation or hot compresses, for 20 minutes three times a day and encouraged active circumduction exercises is suggested. These exercises should be carried out as frequently as a few minutes every hour in order to prevent early limitation of motion, which will occur and will be very difficult to correct after actual contraction and adhesions have developed. If the hemarthrosis is associated with a fracture of the neck of the humerus, the use of a hanging cast and encouraged active circumduction exercises with the added traction afforded by the cast minimizes the disability and greatly improves the prognosis.

ANALGESIC AGENT FOR OFFICE PROCEDURES

To the Editor:—*What risk of explosion is involved in using trichloroethylene (Trilene) analgesia for office cautery or conization? Do you have any other suggestion for analgesia for these procedures?*

M.D., Michigan.

Answer.—Trichloroethylene is noninflammable and nonexplosive when mixed with air or oxygen in concentrations and at room temperatures likely to be used for anesthesia purposes. It should present no risk when used as an analgesic agent for cautery or conization in the office. One caution should be remembered: If direct cautery is used in the mouth during trichloroethylene administration, phosgene will be produced, which is toxic and injurious. For cautery used anywhere in the body other than the respiratory tract, trichloroethylene is safe from explosion. Since analgesia may be readily produced with trichloroethylene vapor, several types of apparatus have been introduced using this drug. For an office procedure such inhalers as the Cyprane inhaler or the Duke inhaler permit air or oxygen or nitrous oxide and oxygen mixtures to be inspired through an inspiratory valve, and by the manipulation of a control lever more or less trichloroethylene vapor may be inspired along with the air or gas mixture. The low volatility of trichloroethylene renders the open mask method difficult. For office procedures trichloroethylene is probably the best analgesic agent available. Those cases requiring full anesthesia can best be handled by other agents such as various local agents, gases such as nitrous oxide, thiopental sodium, or thiamylal sodium.

AIR CONDITIONING

To the Editor:—*I would like an opinion on the ideal climate for a public building in which persons in summer dress will read, eat, and dance during the summer, when the temperature may be often over 100 F. A consultant writing in* The Journal *for Sept. 20, 1952, page 257, suggests the maintenance of the temperature at 3 to 10 degrees cooler than the outside temperature, narrowing the differential as the outside temperature rises. We liberalized this limit to allow a 10 to 20 degree difference and still found the building uncomfortable when the outside temperature reached 105 to 113 F. Such weather resulted in indoor temperatures of over 100 F with a relative humidity of 50%. Is it healthful to maintain a constant relative humidity of 50% as the air-conditioning equipment manufacturer has suggested, or should this be varied? The manufacturers suggest the constant comfort zone of 78 to 80 F at 50% relative humidity. Should we follow this recommendation or vary the temperature upward as the outside temperature rises? Are there dangers to health in maintaining the above comfort zone when persons go in and out of such artificial climate several times daily?*

A. McChesney Evans, M.D., Columbia, Mo.

Answer.—The complexities of air conditioning set forth in this query may not be encompassed fully in this department of The Journal. The chief difficulty centers about the "comings and goings" of occupants of this artificial climate. The statement that with increasing outside temperature the differential between that and the temperature of the air-conditioned space should diminish is fundamental. On that point, Witheridge (in Patty, F. A.: Industrial Hygiene and Toxicology, New York, Interscience Publishers, Inc., 1948, vol. 1, p. 112) advises: "Brief stays of less than a half-hour call for differentials in the neighborhood of 5°, while occupancy of several hours will permit greater differentials, perhaps 8 to 10° F." Practically, it would be absurd to argue that at the excessively high temperature of 113 F comfort would be greatly served merely by reducing the indoor temperature by 3 to 10 degrees; notwithstanding this, the operation of the air-conditioning system at 78 F would prove undesirable for those persons frequently in and out of the conditioned space.

No contradiction of this rule is offered by the fact that in winter persons often leave a space heated to about 80 F and enter a near-zero environment additionally garbed only in overcoat and hat. Through gradual adjustment in the early winter, the human body is conditioned to such changes. Even so, foundry moulders working in winter in temperatures above 100

F, on departing to clothes-change houses nearby, have suffered pneumonia in epidemic numbers with deaths. Although the advantage resides with those who long occupy air-conditioned spaces with temperatures much reduced from that of the outside area, respiratory conditions including infections and exacerbations of such conditions as neuritis, bursitis, and myositis readily develop in many such persons. In the opposite situation, persons leaving air-conditioned spaces with relatively low temperatures and entering an environment of high temperature undergo a condition of thermal shock, immediately manifested in bodily depletion simulating malaise and involving measurable disturbances in basal metabolism. Under an ideal, but highly impractical situation, this transition to and from an air-conditioned space should be graduated, perhaps in three or four stages, so that physiological adjustment might be gradual.

Under the circumstances described, much may be accomplished by clothing adjustments. In many air-conditioned spaces, particularly if there is excessive air motion, added garments are necessary, especially among women. The divestment of these garments aids the physiological state on reentering the hot outer air. Humidification of the air is less important to health than was earlier contended. As to comfort, the degree of humidity may be more important but still is not fundamental. Some investigators, with respect to air conditioning in summer, advise merely dehumidifying the air to a low point without effort to lower temperatures, but this may give rise to an unpleasant sense of chilling owing to increased evaporation. In any event, a humidity between 40 and 60% is regarded with favor.

In over-all appraisal, in the presence of any outside temperature above 100 F a depression to 78 F in the conditioned space definitely does not serve the best interest of persons going and coming in such space. Inevitably, protestations will arise, and abnormal states are likely to appear if the number of persons so exposed is considerable.

MYOCARDIAL INFARCTION

To the Editor:—*A man, aged 46, one year ago had a posterior myocardial infarction followed two weeks later by an anterior infarction. He then had intractable pain and mild hypotension for six weeks, since when he has had mild substernal distress on exertion or in presence of emotional upsets. He now has no dyspnea on ordinary exertion, has few ectopic beats, and is normotensive and in normal weight range. Would a regimen prescribed vary appreciably from that for a more nearly "average" case? Is the prognosis considerably worse because of the second infarction? Please comment on these points: 1. What is the desirability of any dietary measure, including rice diet and low cholesterol diet? 2. Do periodic serum cholesterol determinations have any prognostic value? 3. In prolonged use of an anticoagulant, what is the best one to use, if prescribed, and what is the method of control? 4. Does a momentary feeling of suffocation at irregular intervals, apparently not connected with exertion or tension, have any significance? 5. What are the early signs or symptoms of progressive myocardial degeneration?* *M.D., Iowa.*

Answer.—Assuming all other factors are the same, each additional myocardial infarction makes the outlook of the patient worse. Among the factors that would influence prognosis are the degree of coronary artery sclerosis, the development of collateral vessels, the size of the infarct, and the location of the infarct, which would in turn be important in arrhythmias, mural thrombi, and possible embolism.

1. Rice diet has no value in a patient without hypertension or congestive failure, and low-cholesterol diets in practice have not been very effective in lowering cholesterol or preventing progression of arteriosclerosis and its sequels. 2. Periodic cholesterol determinations are not specifically helpful in giving the prognosis of myocardial infarction unless they demonstrate xanthomatosis and extremely high cholesterol levels, in which event the prognosis would be worse. 3. There is no complete consensus on the prophylactic use of anticoagulants in persons who have had myocardial infarction. If it is done, it requires the most painstaking and accurate control of the patient and control of prothrombin level if serious accidents are to be avoided. Thus it requires a very accurate laboratory. The details of the problem, presented by a group that strongly favors the use of anticoagulants in myocardial infarction, are found in the book "Myocardial Infarction, Its Clinical Manifestations and Treatment with Anticoagulants" (Wright, Marple, and Beck: New York, Grune & Stratton, Inc., 1954). 4. The significance of a momentary feeling of suffocation would have to be determined by the circumstances attending it. Such manifestations generally are seen in fatigue, tension, hypoglycemia, and the like. It is much likelier to be connected with tension than it is to be a manifestation of transient left ventricular failure, though that possibility cannot be excluded on the evidence presented. 5. The early signs and symptoms of progressive myocardial degeneration are those of heart muscle failure, beginning with shortness of breath on effort, progressing to shortness of breath at rest, and usually ending with severe signs of fluid retention.

POLLEN ALLERGY IN BRITISH COLUMBIA

To the Editor:—*A patient who has an allergy problem is planning to move to British Columbia, and she is anxious to pick an area there that will provide as much relief as possible. I would appreciate information about pollen and the incidence of allergic manifestations in the areas of Terrace, Smithers, Vanderhoof, and Prince George.*

Loren F. Blaney, M.D., Denver.

Answer.—Pollen records are available for only two towns in the whole province of British Columbia. Conditions in these places, on the very southern edge of the province, could hardly represent conditions in the mountainous areas mentioned, which are 300 to 400 miles farther north. This patient, whose skin reactions have been submitted, is probably clinically sensitive to Russian thistle (Salsola pestifer) and related plants, to the various sagebrush (Artemisia) species, and, possibly, to ragweed (Ambrosia). The meager information available regarding the hay fever flora of British Columbia indicates that these plants are found only in isolated patches anywhere in the province. Unless the four communities mentioned are in agricultural areas, there could be no Russian thistle, burning bush (Kochia scoparia), carelessweed (Amaranthus), ragweed of any kind. Otherwise, sagebrush would be the only possibility, and the hazard from this would not seem to be very great. Ragweed relatives represented on the test sheet are cocklebur (Xanthium) and false ragweed (Franseria acanthicarpa). Pollen that normally interreact with Russian thistle are burning bush and carelessweed. The Artemisia genus is represented by mugwort and coastal sagebrush. The latter is found only in California. Oak trees are absent from the mountainous portions of British Columbia. Dandelion pollen causes reaction in this patient only because of its close botanical and allergenic relationship to sagebrush and ragweed. The pollen is not wind-borne. Only fragmentary information is available as to the incidence of allergic diseases even in the populous parts of the United States; certainly none in the remote area here considered.

LOCAL USE OF LEAD OR TIN ACETATE

To the Editor:—*I am interested to know whether the local application of lead acetate or tin acetate results in any toxic manifestations.* *M.D., New York.*

Answer.—Application of either lead or tin acetate to the unbroken skin causes no harmful effects of consequence. Percutaneous absorption is unlikely. In general, only some organic lead compounds penetrate the skin. Damaged skin may react differently as to absorption, chiefly with lead, the more toxic of the two metals mentioned. However, the local application of such metallic salts is not wholly unaccompanied by physiological response. Rothman notes: "Salts of lead, tin, copper, arsenic, bismuth, antimony, and mercury tend to form compounds with the fatty acids of the sebum. Thus an originally lipid-insoluble compound in aqueous solution may be transformed on or in the horny layer into a lipid-soluble metal oleate. The percutaneous absorption, then, quantitatively depends on this transformation. The same reaction may take place outside the body to a larger extent if the heavy metal or its salt is incorporated in ointment bases which contain fatty acids. This is one reason for the increased absorption of heavy-metal salts from some ointments as compared with their absorption from aqueous solutions."

REMOVAL OF APPENDIXES

TO THE EDITOR:—*In setting up a tissue committee in a new hospital, we are confronted with the problem of removal of normal appendixes. If one places "chronically inflammed appendix," "fibrotic appendix," and appendix containing pinworms in the category designated normal, what is a permissible percentage of normal appendixes removed as a sole procedure by a surgeon over the course of a year and what is a good rate for a 300 bed, nonteaching general hospital as a whole? To what extent could these figures be modified in the case of a physician dealing mainly with young children, in whom the diagnosis is more difficult and the dangers involved in a case of appendicitis in which operation is not performed are probably greater? As a final question, I am interested in your opinion regarding appendectomy as an elective procedure for what are said to be recurring slight attacks of appendicitis.*

M.D., Canada.

ANSWER.—Probably most cases of acute appendicitis are due to obstruction of the free flow of the appendiceal secretions into the cecum. This obstruction may be due to a fecalith or some other foreign body in the lumen of the appendix, edema of the mucosa, or anatomic factors dependent on a long and tortuous appendix with kinking and adhesions. As a result of the continued secretion by the mucosa of the appendix, the pressure within the appendix rises and vigorous peristalsis in the appendix is induced with the production of a colicky type of pain. In this early stage of appendicitis there may be no pathological changes in the mucosa or muscularis of the appendix. However, as the pressure within the appendix increases, impairment of the blood supply to the appendix results, leading to gangrene and perforation if the process is acute or to fibrosis if the tension subsides. Inflammatory changes in the appendix are thus evidence that the process has gone beyond the stage of simple obstruction. It is maintained that no mistake has been made when an appendix is removed that fails to display inflammatory changes. Pathological changes in the appendix cannot be considered the sole criteria of the advisability of appendectomy, although they are present in the overwhelming majority of cases. It is good surgical judgment to remove an appendix when there is a history of recurring mild attacks of appendicitis, even though at the moment the patient is symptom free. The hazard from acute appendicitis is still sufficiently great that it is unwise to adopt regulations that might interfere with early operation on these patients. In addition to the above information, the article by Dr. George W. Tipton, "The Tissue Audit Committee in an Open Staff Hospital: Three Years' Results from Brackenridge Hospital" (*Bull. Am. Coll. Surgeons* **39**:159 [July-Aug.] 1954), may be of interest.

PLACENTAL TRANSMISSION OF THIOPENTAL SODIUM

TO THE EDITOR:—*Kindly supply information pertaining to thiopental (Pentothal) sodium and its passage through the placenta to the baby in cesarean sections. A paper was presented at the Annual Meeting last June by someone from Denver regarding this subject. In the particular instance involved 0.5 gm. of thiopental sodium was given a patient and a cesarean section carried out. Administration of the anesthetic was started at 8:14 a. m., and the operation began at 8:17 a. m. The baby was delivered at 8:21 a. m.; I would like to know the amount of thiopental sodium that could possibly reach the baby in that interval of time.*

Albert B. Kump, M.D., Bridgeton, N. J.

ANSWER.—According to studies of placental transmission of thiopental sodium (Hellman and others: *Am. J. Obst. & Gynec.* **48**:851, 1944), the anesthetic agent passes the placental barrier in rather small amounts up to the first five minutes. Within 10 to 12 minutes the concentration of thiopental sodium present in the fetal circulation will equal that in the mother's blood. Although the clinical experiments and laboratory measurements referred to here did not happen to include a patient who received 0.5 gm. of thiopental sodium and was then delivered by cesarean section seven minutes later, they did include the following cases: 1. Administration of 0.7 gm. of thiopental sodium intravenously in five minutes resulted in a maternal blood level of 3.9 mg. of acid thiopental per 100 cc. At this same time the infant's blood level was 0.8 mg. per 100 cc. 2. Administration of 0.35 gm. of thiopental sodium intravenously in seven minutes resulted in a maternal blood level of 2.4 mg. of acid thiopental per 100 cc. At this same time the infant's blood level was 1.25 gm. per 100 cc. The level of thiopental sodium present in the infant's blood after seven minutes is about one-half that in the maternal blood.

APPLICATION OF "CONTINUOUS HEAT"

TO THE EDITOR:—*Many orthopedists are in the habit of ordering continuous heat, dry or moist, to infections or joint injuries. Such an order for continuous heat may be applied for quite a number of days. Over the past few years I have developed some reservations about continuous heat, particularly now that electric heating pads are so much in use, and have wondered whether intermittent heat applied for two hours on and one hour off might not accomplish as much as continuous heat and also eliminate the hazards of skin maceration and burns. Is there some particular virtue in continuous heat that intermittent heat cannot accomplish, and is there any potential harm in applying continuous heat to tissue with conditions, such as sprain or cellulitis, in which heat is indicated?*

M.D., Missouri.

ANSWER.—The term "continuous heat," when applied to use of hot, wet packs, is a misnomer. Usually packs are not changed frequently enough, and so actually the heat is not applied "continuously." It is usually desirable to apply hot compresses that are dipped in water at 107 to 115 F for from 30 to 120 minutes at a time. Satisfactorily increased temperature and blood flow in the extremity can be expected only if the compress temperature is maintained by either frequent changes or external heatings. It has been shown that the temperature increases and decreases in an extremity encased in hot compresses as does the temperature of the compress. It would generally seem desirable to allow brief periods without moist heat in order to avoid maceration or, if infrared energy is used, in order to avoid excessive skin drying or burns.

MEDICINAL AND OTHER USES OF THE HORSE CHESTNUT

TO THE EDITOR:—*Are horse chestnuts poisonous to human beings? If not, do they have medicinal value?*

Richard A. Leonardo, M.D., Rochester, N. Y.

ANSWER.—The horse chestnut tree (Aesculus hippocastanum L.; family Hippocastanaceae), a native of Asia, was introduced several centuries ago to Europe and thence to America, where it is very widely cultivated as an ornamental plant. In America, this adventive species has become even more widely known than the native species of Aesculus, commonly called "buckeye." The contents of the large seeds, within a hard shell, consist about one-half of starch. The seed also contains a relatively large amount of tannins, glucosides, and saponins, however, which renders it not only inedible but poisonous when raw, although the poisonous principles have been identified and put to a rather restricted medicinal use. Both the horse chestnut and the native buckeyes have been reported to be poisonous to humans and to livestock. The bark contains a larger proportion of active principles, including escin, a strongly hemolytic saponin that has been put to occasional medicinal use; several glucosides, also of some small medicinal importance; and considerable tannin. Infusions of horse chestnut bark have been used as a home remedy since earliest times but have never become official. The seeds have been used extensively for food by native peoples of the Orient and by Europeans during times of famine, after leaching out the bitter and poisonous principles and roasting the starch. They have also been used as stock food, after proper treatment. The seeds contain up to 5% of oil, which has been extracted on a commercial basis in Europe. During World War I, horse chestnut seeds were an important source of starch for alcohol and acetone fermentation, but in normal times, of course, cheaper and more dependable sources of starch are readily available. A comprehensive and relatively recent sum-

mary of the medicinal and other uses of the horse chestnut has been written by P. Peyre ("Sur les marronniers indigènes et exotiques," Paris, Jouve & Cie, 1943), and from this source may be obtained many further details.

BODY ODOR

To the Editor:—*A Negro man complains of excessive body odor, resembling that from Escherichia coli. This is not confined to the hairy area or to the breath but appears to be coming from the sweat glands of the skin. The cause does not appear to have to do with the teeth or hygienic neglect in bathing. Blood cell counts and urinalysis are normal. Could the factor be found in any type of blood chemistry investigation? Would you suggest a therapy?*

Barnwell R. Baker, M.D., Biltmore, N. C.

Answer.—Body odors are usually grouped under two types: acquired and hereditary. The first is a product of such foods and drugs as garlic, onions, asafetida, and marihuana. The occupation, personal hygiene, and environment also play an effective role. The hereditary type is a racial characteristic. To Asiatics, Europeans and Westerners have a distinctive, pungent odor; Caucasians think that all other groups have a disagreeable odor. The question is vague, as a sharp differentiation is not made between the patient's complaint and what was actually detected by the examiner. Besides these factual odors there is also a condition called bromidrosiphobia, in which the patient complains of body odor although it cannot be detected by others. This answer will be limited to the consideration of odor of Esch. coli that is not confined to hairy areas or breath but emanates from the sweat glands. This patient should be examined for the following conditions: (1) some low-grade inflammatory condition of the gastrointestinal tract with unconscious expulsion of flatus; (2) fistulous tracts—anal, rectal, ureteral, or abdominal; (3) lack of thorough cleansing after defecating, especially if there is a tendency to loose stools; and (4) paronychial infection of fingers. Blood chemistry does not seem to play any significant role. The major emphasis of treatment should be placed on finding the source, real or imaginary. If real, remove the cause. If there is disease of the gastrointestinal tract, change the bacterial flora with sulfonamides combined with antibiotics and give large doses of Lactobacillus bulgaricus.

SEBACEOUS CYSTS

To the Editor:—*I would like information on the prevention of a hereditary tendency toward sebaceous cysts of the skin. A boy, 5 years of age, was born with a small subcutaneous nodule just above the right eyebrow. At 2 years of age this had increased to the size of an olive. Removal with the patient under general anesthesia showed it to be cystic and to contain chrome-colored, semifluid material. Microscopic diagnosis was sebaceous cyst. During the past year this child has had several episodes of painless swelling and closure of one auditory meatus by a sebaceous cyst in the integument lining the canal, which has spontaneously ruptured and discharged. There is, at times, an accompanying swelling of the lymph nodes of the posterior cervical chain. The child's father, aged 35, has been repeatedly troubled for as long as he can remember with pustular acne, occasional boils, and infected sebaceous cysts of his face and neck, which have led to much scarring. Two other children, both girls, have shown no tendency as yet to sebaceous cysts.* *M.D., California.*

Answer.—The only way to prevent hereditary tendencies toward any condition is for one to choose his ancestors with more care. This child is not necessarily doomed to a life of recurrent, painful infections, cystic acne, etc., like his father. Although there is no way to prevent cyst formation, it should be possible to hold to a minimum secondary infections in his lesions and so prevent discomfort and scarring with the judicious use of systemically administered antibiotic agents. The decision as to when to destroy the sebaceous cysts, by either surgical excision or electrosurgical means, is guided by the size and location of the lesions. Some are removed solely for cosmetic reasons, others because, owing to their locations, they are subject to repeated injury or irritation.

STERILITY

To the Editor:—*I have heard that the wearing of constricting or support-type underwear by men is thought to be a factor in sterility. Are any scientific data available on this question?*

M.D., New York.

Answer.—There are no convincing data to support the belief that there is a relationship between the wearing of brief-type shorts and sterility. Dr. John MacLeod, professor of anatomy at Cornell University Medical College, has made extensive observations on medical students who had semen analyses before and after wearing brief-type shorts, and he reports there was no significant variation in the semen analyses.

DISCHARGE FROM THE NIPPLE

To the Editor:—*A 44-year-old woman, gravida 3, para 3, for the past 10 years has had a serous, clear drainage from her right nipple. This drainage was at first intermittent but for the past three years has been continuous. Additionally, she has had bleeding from the nipple for periods of one week, intermittently, for the past four years. The bleeding is rather heavy. There is no visible lesion or incrustation on the nipple and no tumor palpable in the axillas or in either breast. There is no visible retraction of skin over the right breast. Her left breast has caused her no trouble at any time. Her family physician advised her to leave the breast alone as long as it does not get worse. Realizing that this may be a low-grade carcinoma or intraductile papilloma that has already existed over a period of 10 years, I am reluctant to advise her to have an exploration of the breast. Yet I feel this should be done. What would be sound advice? She had a pelvic laparotomy in 1947, with an abdominal supracervical hysterectomy and bilateral partial oophorectomy, for metrorrhagia and vaginal discharge due to uterine fibroids. She had an appendectomy in 1929 for acute appendicitis. Prior to the hysterectomy, she had menorrhagia for a long time. Her menses had always been regular prior to the surgical menopause in 1947. There had never been any masses in the breasts or cysts that formed from month to month with the menses.*

James W. Pick, M.D., West Bend, Wis.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—Kilgore, Fleming, and Mario Ramos (*Surg., Gynec. & Obst.* **96**:649 [June] 1953) reported on 190 patients with nipple discharge. In about one-sixth the discharge either was grossly milky or contained normal secretory elements microscopically. No cancer was observed in these women, nor was the discharge a forerunner of cancer. In 55 women with serous, nonbloody discharge, 3 had papillary disease and one had papillary disease plus cancer—about 8% with demonstrated papillary lesions. Blood-containing discharge was observed in 103 patients. Of this group 31 refused treatment, and as far as is known cancer developed in none of these women. However, 17 of the 103 women with bloody discharge had cancer or "debatable" cancer when first operated on. Four of the 14 patients with cancer and 2 of the 3 with debatable cancer had no mass that could be felt. No method of locating and locally removing a single lesion of papillary disease in the absence of a palpable lump, is uniformly successful, and if such a lesion is found the chance of leaving other, undiscovered lesions elsewhere in the breast is considerable. For these reasons, a woman past the age of 40 with blood-containing discharge or demonstrated papillary disease should be advised to consider the acceptance of mastectomy (extended to radical operation if cancer is discovered). Even younger women with multiple lesions are offered the same advice.

Answer.—This patient may have intraductal papillomatosis. Most authorities feel that these papillomas are benign or malignant from the start and do not change over. The likelihood of carcinoma existing in this breast over a period of four years is therefore small. Often those segments of breast from which the bleeding is coming can be identified by finger-tip pressure at intervals about the areola, watching to see where the pressure produces the discharge. In other instances it is possible to thread

a small probe into the duct from the nipple from which the blood is issuing. If either of these maneuvers can be accomplished, that segment of the breast can be excised not only for microscopic study but to put an end to the unpleasant discharge. When the duct cannot be identified and the discharge is a problem, 1,500 r of x-radiation applied over the breast in fractional doses will often dry it up. Simple mastectomy is not justified, since if a malignant papilloma exists radical mastectomy is the treatment of choice.

GALACTORRHEA

TO THE EDITOR:—*A 23-year-old white woman nursed her second baby for only a short while. Since that time, small amounts of a milk-like substance can be expressed from her right nipple. Her right breast is somewhat tender but shows no anatomic anomalies. There is no mastitis and no psychic or metabolic disturbance. The patient failed to have the condition treated for about two years. After that time she received a diet rich in protein and vitamins with reduced fluid, fat, and carbohydrate intake; diethylstilbestrol; atropine; and, finally, testosterone, intramuscularly and orally. However these regimens seem to have only a transitory effect. At present she receives testosterone, 100 mg. intramuscularly once a week, and testosterone propionate (Oreton), 10 mg. twice a day. So far there are no signs of masculinization, although her last menses were a little scanty. Should the treatment be continued; if so, for how long? Is there any other treatment that could be beneficial? How about x-rays? She occasionally feels a very slight drawing pain in her right breast, while the left one is absolutely without symptoms.* *M.D., New Jersey.*

ANSWER.—True persistent secretion of milk or galactorrhea is rare. It usually occurs after the second or subsequent weaning, and little is known about its etiology. In cases of Frommel's disease the galactorrhea is associated with atrophy of the uterus, absence of menstruation, and a urinary gonadotrophin level of either zero or less than 6 mouse units for 24 hours. Argonz and del Castillo (*J. Clin. Endocrinol.* **13**:79 [Jan.] 1953) reported on four patients who showed a syndrome characterized by galactorrhea, amenorrhea, and low values for urinary gonadotrophin. This had no relation to pregnancy. Even though evidences of estrogenic insufficiency were found, substitution therapy modified the clinical picture only temporarily. Treatment of galactorrhea is unsatisfactory. Mastectomy has been advised in persistent cases, but this heroic measure is not recommended. If the patient is not uncomfortable, all hormone therapy should be discontinued. A curettage should be performed, as this is known to have effected a cure in one case. V. Valverde Pinedo (*Acta gynaec. obstet. hisp.-lusit.* **2**:295, 1952) reported the case of a woman who had breast secretion for two and one-half years. Estrogen treatment failed to give relief, but curettage resulted in complete cessation of the flow of milk. The curettage was done a few days before an expected menstruation and revealed a proliferative phase. The author suggests that the flow of milk was due to a deficiency of the pituitary luteinizing hormone, because of the association between the ovarian hormones and prolactin.

BRUISING DURING PREMENSTRUAL WEEK

TO THE EDITOR:—*In many women during the premenstrual week black and blue marks tend to develop from slight or unrecognized traumas. In some cases there is complaint of aches and soreness in the muscles and joints of the pectoral and pelvic girdles, with sciatic shooting pains, the whole being compared to the similar soreness and pains in these regions during the last month of pregnancy. What work has been done on this bruising tendency during the premenstrual week?*

M.D., North Carolina.

This inquiry was referred to two consultants, whose respective replies follow.—ED.

ANSWER.—As far as is known, there are no published studies of a bruising tendency during the premenstrual week. A special bruising tendency a few days before the onset of the menses is not common. The customary treatment for premenstrual tension may help patients in whom there is a tendency to bruise and develop blue marks and also those with various pains that appear premenstrually, because such therapy has relieved many women of odd symptoms that occur at this time as well as the customary ones such as headaches, abdominal distention, nausea, fulness of the breasts, edema, and emotional disturbances.

ANSWER.—Considerable experimental work has been done in this field, and it is thought that there is no change in the coagulability of the blood or in the platelet count. It is believed that the patient bruises easily because there tends to be an increased capillary permeability, to a minimal degree. It is possible that these spider hemorrhages may also be dependent on certain hormonal influences, namely, either withdrawal of estrogens or withdrawal of progestogens just prior to menstruation. There are two peaks of estrogen ascendency, one at the time of ovulation and the other a few days prior to menstruation. Estrogens support the endometrium, and their withdrawal causes cellular dissolution. The work of Browne, Venning, and Henry and of others has shown that uterine bleeding will occur one to four days after withdrawal of progesterone and that it is not necessary for a progestational endometrium to come about for bleeding to occur. It would seem that, as these petechial hemorrhages often occur just prior to menstruation, a hormonal relationship could be postulated. It is best to advise the patient that the condition is not serious and no treatment is recommended; if this does not suffice, small daily doses of progesterone, hypodermically, may be of value.

DUODENAL ULCER

TO THE EDITOR:—*An internist in this community treats duodenal ulcers with twice-weekly intramuscular injection of 5 mg. of desoxycorticosterone. I inquired about the rationale of this treatment, and he explained that the adrenal glands were related to gastric hypersecretion, as exemplified by the fact that ulcer patients do not tolerate cortisone. Therefore these injections of desoxycorticosterone supposedly inhibit secretion. I would appreciate comment on this treatment.*

M.D., California.

ANSWER.—A small dose of desoxycorticosterone has little or no effect on gastric secretion either directly or through inhibition of function of the anterior lobe of the hypophysis. Both corticotropin and cortisone stimulate gastric secretion and increase the output of hydrochloric acid and pepsin by from 50 to 100% above the normal level. Presumably corticotropin acts by increasing the secretion of cortisone from the cortex of the adrenal glands. The administration of large doses of cortisone does inhibit the function of the anterior lobe of the hypophysis, causing a decrease in the liberation of corticotropin. There is, however, no evidence that 5 mg. of desoxycorticosterone has a similar effect. At the present time, there is no rational basis for the treatment of duodenal ulcers by the method suggested in this question.

BRONZING IN CLOSTRIDIAL INFECTIONS

TO THE EDITOR:—*What is the pathogenesis of the bronzing characteristic of clostridial infections?*

Edwin R. Kaback, M.D., Otisville, N. Y.

This inquiry was referred to two consultants, whose respective replies follow.—ED.

ANSWER.—Clostridia, and especially C. perfringens, which is often the dominant species in gas gangrene, produce toxins that are powerfully hemolytic. They do not produce pigments, and the source of the bronzing is most probably hemoglobin. The crepitant subcutaneous or deep areas of intense, hemorrhagic, edematous, gaseous cellulitis so characteristic of the disease provide much free hemoglobin in a profoundly altered oxidation-reduction environment that at times may convert much of it to the nonferrous brownish pigments.

ANSWER.—Possibly the bronzing characteristic referred to can be explained on the basis of an oxidizing enzyme, as in the case of Addison's disease. Bloch (cited by Best, C. H., and Taylor, N. B.: Physiological Basis of Medical Practice, ed. 5, Baltimore,

Williams & Wilkins Company, 1950, p. 809) concluded that dihydroxyphenylalanine, which he called dopa, was the precursor of melanin, the conversion being brought about by the oxidizing agent. This would assume that there is a deficiency of the cortex and that a greater amount of dihydroxyphenylalanine is converted to melanin and less into adrenalin. Bronzing is sometimes observed in diabetes.

NEUROSYPHILIS

To the Editor:—*Kindly outline the treatment of neurosyphilis with chloramphenicol (Chloromycetin) and also discuss the efficacy of this drug.*

L. Gouguet, M.D., Sacramento, Calif.

Answer.—There is no satisfactory information on the treatment of neurosyphilis with chloramphenicol. This, together with other antibiotics of the tetracycline series, has some treponemicidal effect, but it is much less marked than that of penicillin; no one of these antibiotics can be considered to replace penicillin. Information concerning the treatment of any form of syphilis with chloramphenicol is very fragmentary, and no estimate of its real value is available. In view of the known tendency of chloramphenicol to produce aplastic anemia (and in spite of the fact that this is a rare occurrence) most chemotherapists would agree that the use of this particular antibiotic should be reserved for such serious, acute infections as typhoid, in which its superiority over other antibiotics has been demonstrated.

HYPERTENSION

To the Editor:—*A 48-eight-old, white, single woman has essential hypertension ranging from 190-140/110-130 mm. Hg with recent onset of anginoid pains in the left arm and neck on exertion. Her condition is controlled by glyceryl trinitrate (nitroglycerine). There is no history or electrocardiographic evidence of myocardial damage or conduction irregularities. This patient is interested in moving to Mexico. She has asked what effect high altitudes or lower barometric pressures would have on her blood pressure and cardiac status. Her condition usually has a moderately good response to any hypotensive agent for about one month and becomes refractory thereafter. How should I advise her?* *M.D., Ohio.*

Answer.—This patient has rather severe hypertension and may be showing symptoms of myocardial ischemia as indicated by the anginoid pain controlled by glyceryl trinitrate. She could probably adjust to the higher altitude of Mexico City, although several weeks might be required. It is doubtful that her arterial pressure would be significantly influenced. It would seem wise for her to be in some place where a physician experienced in the use of hypotensive drugs is readily available.

REPELLENT FOR BITING INSECTS

To the Editor:—*What chemicals or preparations will repel the common tick (Ixodes)? Is there any substance that may be applied to the clothing to discourage their attacking the human body?*

Charles E. Long, M.D., Memphis, Tenn.

Answer.—The best all-purpose repellent, not only for ticks but also for other biting insects, that may be safely used both topically and as an application to clothing is compound dimethyl phthalate solution, U.S.P. XIV.

COCAINIZATION OF SPHENOPALATINE GANGLION

To the Editor:—*1. Is cocainization of the sphenopalatine ganglion of any value in the treatment of acute herniation of a nucleus pulposus in the lumbosacral region? 2. Is there any anatomic or physiological relationship between these structures? 3. What is the rationale of such treatment?*

Howard K. Ente, M.D., Westport, Conn.

Answer.—1. No. 2. No. 3. None.

NONSPECIFIC URETHRITIS

To the Editor:—*The answer to a query in* The Journal, *Nov. 27, 1954, page 1300, concerning the treatment of nonspecific urethritis aboard a Navy ship omitted one important aspect.*

When urinary symptoms are absent, the prostate is firm, and there is no evidence of urethral stricture, most cases of so-called nonspecific urethritis are expressions of an anxiety state. The usual patient is one who has been reared under strict parental and religious control. Following induction into the service he is bombarded with venereal propaganda officially and by his shipmates, and after his initial indiscretion he is convinced that he has venereal disease. His waking hours thereafter are spent looking for evidence of venereal disease by constantly stripping the urethra. A series of drugs given orally and by injection may temporarily improve the condition but frequently will aggravate the anxiety state, with persistence of the urethritis. Patient reassurance with explanations of the physiology involved should be the primary therapeutic attack. Frequently these patients are fearful of being impotent, sterile, or unable to void or of cancer developing. Treating the urethritis without treating the anxiety component, needlessly, and sometimes hopelessly, prolongs the therapy. The urogenital mucosa in these patients responds readily to all sexual stimulation; there is intense activation of the involved glands. Hence anything of a libidinous nature, including conversation or reading, must be avoided. A reorientation of the patient's thinking is indicated to dispel his anxiety and cure his urethritis.

Commander Stanley J. Okulicz (MC), U. S. N.
Amphibious Group Three
Fleet Post Office, San Francisco.

To the Editor:—*I read with interest the letter concerning the treatment of nonspecific urethritis in* The Journal *of Nov. 27, 1954, page 1300. I am a youngster in the family of physicians and wish to emphasize that this letter is written with a deep sense of humility, but with some hope that it may aid a few in the treatment of what appears to be a disease of increasing morbidity. The answer to the above query unquestionably is correct in suggesting the identification of causative organisms and sensitivity studies thereon. However, in treating large numbers of men, and with laboratories of limited extent as found aboard ships, such an approach is not practical. A report entitled "Nongonococcic Urethritis in the Male" (Parrino, P. S.:* U. S. Armed Forces M. J. *5:1249 [Sept.] 1954) discusses the problem extensively. Since reading this paper, our small medical department has followed the suggested treatment and has noted a marked decline in the number of therapeutic failures, which had been common previously. The regimen now followed is: (1) 800,000 units of penicillin G and 1 gm. of dihydrostreptomycin sulfate intramuscularly once a day for two days; (2) force fluids; (3) absolutely no "milking" of the urethra by the patient; and (4) careful follow-up with periodic Kahn tests.*

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EXOPHTHALMIC GOITER

To the Editor:—*I always read Queries and Minor Notes with interest and profit. In the Dec. 18, 1954, issue of* The Journal, *page 1545, under the heading "Exophthalmic Goiter," a physician from Portugal reports a case of apparently mild, recurrent exophthalmic goiter in a patient with a basal metabolic rate of +26%. With such a rate, the recurrence must have been mild indeed. I would question the necessity for radioactive iodine in such a case. With the proper postoperative regimen, that is, omitting all stimulants and giving a high caloric diet and 5 drops of Lugol's solution twice a day, the chances are that the basal metabolic rate would be returned to normal within a few weeks; very probably this treatment would effect a cure within a few months. Propylthiouracil, 50 mg. three times a day, would accomplish the same result.*

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